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PROBLEMS OF HYPERSENSITIVITY*

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As is well known, hypersensitivity, or allergy as it is ordinarily called, is a specific type of alteration of the body's reactivity to a given foreign substance, caused by previous contact with that substance. When this alteration has occurred, tissues will be more readily damaged or killed by contact even with amounts of the foreign substance that would be completely harmless to the normal, non-hypersensitive body; and severe constitutional symptoms, and even death, can occur when amounts that are entirely harmless to the normal body enter the blood stream of the hypersensitive one.

The first clear recognition of this remarkable type of altered reactivity was recorded over 150 years ago by Edward Jenner in his description of the accelerated local reaction to vaccination in persons who had previously been vaccinated, or who had previously had smallpox. In spite of the prompt acquaintance of the world with Jenner's celebrated monograph, and though vaccination and revaccination were soon practised throughout the civilized world, Jenner's discovery of this (as he called it) "remarkable . . . disposition to sudden cuticular inflammation" which those who have previously been vaccinated exhibit on revaccination, attracted scant attention for a hundred years, when a similiar observation was made by Robert Koch during his experimental studies on reinfection in tuberculosis in the 1890's. In contrast to Jenner's neglected, clear description of the phenomenon, Koch's observation promptly aroused widespread interest in hypersensitivity. The time was ripe—as is evident from any examination of the climate of thought surrounding Koch's report.

The hypersensitivity observed by Jenner and by Koch was the type now known as the hypersensitivity of infection, or the tuberculin type of hypersensitivity, which differs in numerous ways from the anaphylactic type. During the first decade of the present century, the anaphylactic type of hypersensitivity and several of its injurious effects were discovered, and the very important fact was established that the substances which cause the development of anaphylactic hypersensitivity are antigens, which incite the production of antibodies; and the injurious effects were shown to result from the interaction of the sensitizing agent with its specific antibody.

Following the widespread interest in the anaphylactic type of hypersensitivity that was aroused by those studies, and aided by the development of clinical tests for the detection of sensitizing agents and their antibodies, the number of recognized sensitizing agents to which we are exposed has increased enormously, and continues to increase parallel with the seemingly endless increase in the introduction of new chemical substances into our daily environment, many of which turn out to have sensitizing potentialities. Indeed, the number of different, recognized sensitizing agents to which the population is exposed, has increased to the degree that they now far outnumber the different types of pathogenic micro-organisms as agents of disease. The ever-increasing multiplication of new, useful, but sensitizing drugs forms a particularly serious part of the hazard of hypersensitivity caused by exposure to new natural and synthetic chemicals, for in most instances drugs are administered with the intent that they will be carried by the blood stream in sufficient concentration to the site where they are needed. When hypersensitivity develops under such conditions, vital tissues throughout the body are exposed to the threat of damaging hypersensitivity effects produced by the interaction of antibody with the circulating sensitizing drug. This threat will become a reality at sites where local conditions are favourable to the injurious antigen-antibody reaction. The harmful and even fatal results of this are more common than is ordinarily appreciated, and are a matter of serious concern. One of the large problems relating to hypersensitivity is that of finding a way to protect patients from being gravely injured by hypersensitivity effects of drugs that are administered to help them.

As for the injurious effects that hypersensitivity can produce, it was gradually recognized that far from being only a rare and peculiar phenomenon, as it was first regarded, hypersensitivity is one of the commonest causes of human disease. There has been a steadily continuing increase in types of

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lesions that have been found to be caused by hypersensitivity, and it is altogether probable that still others will be discovered. In the future this may be particularly true in the realm of auto-sensitization,—i.e. sensitization to modified specific substances derived from the individual's own tissues. One or two examples of serious disease states produced by auto-sensitization in man have already come to light, and the condition has been reproduced in experimental animals. The manner of spontaneous development of this phenomenon, and the creation of adequate methods for the recognition of its presence, are problems which will demand increasing attention.

It is now thoroughly well established that hypersensitivity of the anaphylactic type can cause an extraordinary variety of lesions and disturbances of function, including not only anaphylactic shock and the familiar allergic conditions of asthma, hay fever and cutaneous eruptions, but also arthritis, myocarditis, necrotizing-inflammatory arteritis, focal collagen degeneration, pneumonitis, peripheral neuritis, hepatic necrosis, pancreatitis, gastrointestinal pain and diarrhea, tuberculoid lesions, necrosis in lymphoid tissue, thrombocytopenic and non-thrombocytopenic purpura and other important hematological disorders, and three forms of nephritis—ordinary acute proliferative nephritis, focal necrotizing glomerulonephritis, and acute interstitial nephritis—each of which can cause death from uremia. Of these 20 conditions which are now known to be effects that the anaphylactic type of hypersensitivity can produce in man, 15 have been successfully reproduced experimentally in animals by inducing this type of hypersensitivity reaction.

It is clear that important advances have been made, and indeed still are being made, in the recognition of the manifold types of injury that can result from hypersensitive reactions, and in the identification of a great number of sensitizing agents to which we are exposed. In addition, the fundamental fact has been learned that the occurrence of the injurious effects of hypersensitivity requires the interaction of antigen with antibody. While these additions to knowledge are of very great importance, it cannot be too strongly or too often stressed that the actual mechanism by which the antigen-antibody interaction injures tissues is still unknown, and the understanding of the local tissue conditions that are necessary for the production of the different injurious effects still eludes us.

Since the injurious effects of the type of hypersensitivity that we are discussing are now known to result from the interaction of the sensitizing antigen with its specific antibody, one of the most fundamental and important problems with which we are faced is the mechanism by which the antigen-antibody interaction produces its damaging effects. About this, we have virtually no solid information. It has seemed probable that the lesions of hypersensitivity are produced by an injurious agent of some sort that is liberated, in some way, as a result of the antigen-antibody interaction, but neither the injurious agent nor the manner of its liberation has yet been identified. Histamine liberation may possibly account for some of the effects associated with hypersensitivity, such as urticaria; but, as we have stressed before, present information does not permit us to invoke histamine as the cause of most of the lesions that are known to be effects that hypersensitivity can produce—such, for example, as periarteritis nodosa; the marked inflammatory infiltrations which, when present in the heart or kidneys, can cause cardiac or renal failure; the degeneration of collagen; the tuberculoid lesions; or the hemorrhagic, inflammatory-necrotic damage to tissue characteristic of the Arthus phenomenon. None of these injurious effects of hypersensitivity can be produced by the injection of histamine.

Regarding local conditions that determine whether or not a given tissue site will be injured, it is known that different persons, though equally exposed to a sensitizing agent, do not become equally sensitized, and this is true of individual animals of a given species in controlled experiments. While individual differences in the ability to produce antibody are clearly important in these differences in degree of sensitization, it is equally clear that other factors must play an important role in determining whether the presence of antigen and antibody will produce injurious effects, and in determining the sites at which the injurious effects will occur; for when a hypersensitivity reaction is passively induced in normal animals by infusing carefully standardized amounts of an antigen and its antibody into the blood stream, some will develop necrotizing arteritis; some will develop glomerulonephritis; some, tuberculoid lesions; and some, various combinations of these lesions; while in others, no lesions at all will occur. Similarly, in the human being, different individuals who become sensitized to a given antigen may differ markedly in their tendency to develop damaging lesions on equal contact with the antigen. It is a well-known and remarkable fact that both the character of the hypersensitive injury and the site at which it occurs may be very different in different individuals sensitized in the same manner to the same antigen, and exposed in the same manner to it after sensitization. For example, following the ingestion of a given food protein to which the body has been sensitized, one person may always develop urticaria; another, eczema; a third, purpura; a fourth, vasomotor rhinitis; a fifth will regularly have an attack of abdominal pain, vomiting and diarrhea; a sixth will always develop an asthmatic attack; a seventh, an attack of arthritis; in an eighth, ingestion of the protein may regularly precipitate a transient attack of acute nephritis; the ninth may exhibit a combination of two or more of these conditions; and a tenth, though demonstrably sensitized, and exposed to the protein in the same

manner, will experience no injurious reaction. Very commonly, in a given individual the injurious effect of the antigen-antibody interaction will regularly recur in the same form and at the same general site. What the local tissue conditions may be that render a particular tissue site in a given individual more favourable than elsewhere for the occurrence of an injurious hypersensitivity reaction of a particular type, is completely unknown.

The history of science, and of biological science in particular, warns against predicting with confidence the route that will lead most rapidly and successfully to the solution of a complex problem. Though mindful of this, I would look most hopefully to the acquisition of knowledge regarding the mechanism by which the antigen-antibody interaction produces the ill effects of hypersensitivity, and to a clarification of the nature of the local tissue conditions that determine the remarkable individual differences in the localization of the lesions in different individuals. If we knew *how* the interaction of antigen with antibody injures tissue, and if we knew the nature of the local tissue conditions that determine whether or not the injurious interaction will take place at a given site, it might be possible to neutralize the injurious effects specifically, safely and effectively. This would obviously be of inestimable value in abolishing the distressing and dangerous effects of antigen-antibody interaction in the great field of diseases of hypersensitivity.

A SURVEY OF TOXOPLASMOSIS IN AN ONTARIO COMMUNITY*

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THE LITERATURE on toxoplasmosis has grown steadily over the past 20 years, indicating the development of a "toxoplasmosis consciousness" among doctors and veterinarians. The subject has recently been reviewed in the Canadian literature.[1, 2] Over the past ten years, both in Toronto[3, 4] and at the Ontario Veterinary College,[5] studies on this subject have been carried out, but these have been hampered by the difficulty of establishing satisfactory laboratory tests; such difficulties have been both technical and financial. A Sabin-Feldman dye testing laboratory was set up at the Toronto Hospital for Sick Children in 1953, but its services were discontinued after only nine months of operation. Dye test results were obtained through the cooperation of laboratories in the U.S.A. until the establishment of a Sabin-Feldman dye testing laboratory at the Ontario Veterinary College in Guelph in 1959. An alternative serological test, the complement fixation test, has been carried out at the Ontario Provincial Laboratory for the past five years as part of the routine services offered for laboratory diagnosis.

The results of tests from these laboratories have confirmed the fact that infection with *Toxoplasma gondii* is present within the province of Ontario. From the evidence of larger surveys undertaken elsewhere in both temperate and tropical climates[6] such infection is widespread, but largely unrecognized because only rarely does it erupt as a clinical entity and then only sporadically in man. This is not necessarily the case among animals. Nevertheless, it has been suspected that human infection with *Toxoplasma gondii* may be the cause of much of the low-grade morbidity that exists in the area of Canada[2] under discussion. As a necessary preliminary to investigating this possibility, a survey of a sample population is essential, utilizing the Sabin-Feldman dye test which has been shown, up to now, to be the only accurate indicator of past infection in a sample of population. The complement fixation test is not a satisfactory indicator of previous infection, because, besides appearing later in an actual infection than the dye test, it does not persist as long after the infection has been overcome. The hemagglutination test for toxoplasmosis will also be evaluated as a practicable procedure in this type of survey, for its relative simplicity as compared with the dye test could lead to its adoption as a standard diagnostic test. The toxoplasmin skin test has been included in this survey mainly because of its simplicity and availability. There has been, over the past few years, increasing dissatisfaction with the latter as a specific and reproducible test. Feldman[7] feels that there is no satisfactory way to standardize the antigens and that it is questionable whether comparable data can be obtained with different lots or dilutions of antigen.

MATERIALS AND METHODS

A sample of the population of the West Toronto area consisting of the adjacent borders of the counties of York and Peel was studied; this comprised 650 consecutive patients in selected age

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groups, admitted to the Queensway General Hospital, Toronto, and these were drawn in the main from the primary hospital area (see Fig. 1). They were all volunteers who agreed to have skin and serological tests and were not suffering from chorioretinitis or lymphadenopathy which might conceivably have been due to *Toxoplasma gondii* infection.[8] All subjects were interviewed briefly and the information was classified in the following manner: experimental no.; hospital no.; discharge diagnosis; sex; race; religion; birthplace; residence in past five years; present map location cypher; number of persons in household; family pets or domestic animals; febrile; skin test; complement fixation test; hemagglutination test; dye test.

It was felt that collection of information in this manner might suggest some previously unrecognized clue to the possible mode of infection, particularly as so few studies on the serological evidence of Toxoplasma antibodies have taken into account the social and environmental details of the persons being tested. Much of the earlier survey work was carried out on sera collected for other purposes, such as testing for Widal reactions, encephalitis, cold agglutinins, Paul-Bunnell reactions, blood donors, Wassermann reactions and numerous other tests.[6, 9, 10] Only two recent studies have attempted to correlate the serological reaction with details of the personal history;[11, 12] this is surprising in view of the suspected occupational and social influence on the incidence of toxoplasmosis.[13]

THE SKIN TEST

The skin test has no positive value in the diagnosis of an acute case of Toxoplasmosis, as its appearance is delayed following infection. If it is positive in a suspected patient, then a previous infection has occurred, and this excludes the diagnosis in the current illness. In fact, a positive dye test will appear before a positive skin test. On the other hand, it may be a useful tool for investigating the incidence of infection in a survey of population samples, but doubts about its validity in this regard have already been expressed. The material used in this study consisted of antigen prepared from Toxoplasma grown in mouse peritoneum. Both antigen and control material were diluted as supplied ready for use. Intradermal injection of 0.1 c.c. of both antigen and control material was made on the flexor surface of each forearm respectively. Readings were made after 24 and 48 hours; an area of erythema and induration of more than 10 mm., with a negative reaction in the control, was regarded as positive.

SEROLOGICAL TESTS

Specimens of sera were stored in the frozen state until examined, and this period averaged six weeks. They were divided into three aliquots, each being specifically tested by the Sabin-Feldman dye test,[14] complement fixation test[15] and the hemagglutination test.[16]

The dye test is based on the following principle. Toxoplasma organisms have a high affinity for alkaline methylene-blue staining solution. However, in the presence of a specific antibody which acts in combination with an accessory factor, Toxoplasma loses this quality and remains as an unstained organism. The technique is as follows. The sera to be tested are inactivated for 30 minutes at 56° C. It is possible by inactivation to avoid non-specific reactions in low serum dilution. Toxoplasma immune sera appear to retain their titre over a long period if stored at 0° F. or lower. The specific dye test antibody is thermostable. After inactivation the sera are diluted with physiological saline in fourfold dilutions. The diluted serum is then mixed with a Toxoplasma suspension derived from the peritoneal exudate of Toxoplasma-infected mice. This suspension is also mixed shortly before use with a quantity of serum from a healthy person containing accessory factor but devoid of Toxoplasma antibodies. However, this accessory factor differs from the complement (alexin) which is used in the fixation of the complement reaction.

In preparing the dye test the sera are diluted previously, i.e. 1:16, 1:64, 1:256, etc., with physiological saline. From each dilution 0.1 ml. is removed and placed in Wassermann tubes; then 0.1 ml. of the mixture containing Toxoplasma in the form of peritoneal exudate from infected mice, plus accessory factor, is added. After one hour of incubation at 37° C., 0.1 ml. of alkaline methylene-blue solution is added to the tube. The mixture is shaken carefully and immediately examined microscopically to note the dilution up to which the Toxoplasma organisms have remained unstained in a proportion of over 50%. This dilution represents the titre of the antibody. It is observed that intracellular Toxoplasma organisms are not affected by the presence of the antibody, and for this reason only the extracellular organisms are counted.

The complement fixation test used in this survey has been in use routinely at the Ontario Provincial Laboratories in Toronto over the past five years.[15] The materials used were as follows: RH strain *Toxoplasma gondii* was obtained from the Hospital for Sick Children, Toronto, through the courtesy of Dr. T. E. Roy and has been maintained through passages in Swiss albino mice. The antigen was prepared by harvesting the peritoneal fluid from infected mice, centrifuging it, resuspending it and storing it, frozen, until required. When required, the material is thawed and inactivated at 56° C. for 60 minutes, then alternately frozen and thawed several times, ultrasonorated and again frozen and thawed two or three times. The material is now centrifuged at 35,000 r.p.m. for 30 minutes and the supernatant is stored as antigen at 4° C. until used. Immune rabbit serum for use in the complement fixation test was prepared by immunization with an emulsion of chick embryo allantoic membranes infected with RH *Toxoplasma gondii*.

The hemagglutination test is applicable to an increasing variety of antigens, both polysaccharide and protein, and represents an attempt to apply a comparatively simple test for toxoplasmosis which could be generally adopted. Jacobs and Lunde[16] initiated its use with promising results. However, up to the present time insufficient material has been accumulated for proper evaluation and it will not be possible in this paper to do more than suggest its usefulness. The technique utilizes the phenomenon that red blood cells exposed to an antigen become sensitized to a homologous serum. The technique carried out was as follows. The RH strain *Toxoplasma gondii* was the same as that used in the complement fixation test. The antigen was prepared from peritoneal fluid from infected mice, which was harvested and centrifuged and the sediment resuspended. Debris was removed by centrifugation and the supernatant adjusted to the osmotic pressure of physiological saline. The antigen was stored frozen until used. All sera, including normal rabbit sera, were incubated at 56° C. for 30 minutes and absorbed overnight with equal volumes of washed, packed sheep red blood cells to remove heterologous antibodies. Test sera were diluted with normal rabbit serum (dilution 1:50).

The sheep red blood cells (defibrinated) are washed three times. A 3% suspension of red blood cells is made with buffered saline (pH 7.2). Equal volumes of red blood cell suspension and tannic acid solution 1:20,000 are mixed, and the mixture is incubated at 37° C. for 15 minutes. The cells are centrifuged, washed and resuspended in physiological saline, then sensitized with Toxoplasma antigen at room temperature for 15 minutes. After centrifuging and washing, the cells are resuspended in normal rabbit serum (dilution 1:100). Now 0.05 c.c. of sensitized cell suspension is added to 0.5 c.c. of each test serum dilution. These are shaken. This is followed by incubation at 37° C. for two hours and the test is then read. After being shaken again, the test is left at 4° C. overnight and then at room temperature for an additional hour and read again.

CRITERIA FOR SEROLOGICAL POSITIVITY

The criteria required for diagnosis of past infection and active disease differ not only in the level of the significant titre of an individual test but also in the significance of the test itself. There has been general acceptance that the Sabin-Feldman dye test is of greater value in epidemiological surveys, for while development of a significant titre may be delayed up to four weeks after infection, it will persist for many years and thus is suitable for mass surveys. While it would seem reasonable that all positive dye tests should be regarded as significant, this is not in fact universally acceptable, and a minimum titre of 1:16 for evidence of past infection and one of 1:64 for evidence of active infection have become the standard criteria, based on experience and passage of time.

There has been general acceptance that in the complement fixation test a titre of 1:8 or more is necessary before the diagnosis of toxoplasmosis is justified.[10, 15] More recent work has suggested that a lower titre is justified.[17] The distinction between the significance of the dye test and the complement fixation test has already been referred to, and it will be one of the purposes of this survey to test the validity of the assumption that the complement fixation test has no place in mass surveys to detect evidence of previous toxoplasmosis infection.

The hemagglutination test will not be used to diagnose toxoplasmosis in this survey, but rather to compare its results with those of the other two serological tests. Therefore, at the present time we have no definite criteria for serological positivity in this test.

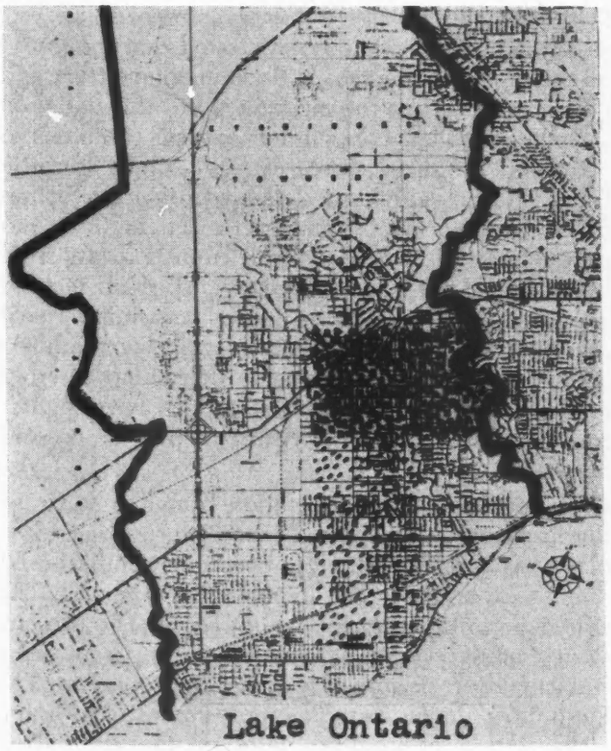

Fig. 1.—Map of Etobicoke Township from which came 85% of the samples. The heavily shaded area contained 40-50% of positive reactors among individuals tested, the lighter area 30-40%. Elsewhere the percentage dropped sharply.

GEOGRAPHICAL LOCATION

The greater percentage (71%) of the 650 sera tested came from the area demarcated on the accompanying map (Fig. 1) in the Township of Etobicoke on the western outskirts of the city of Toronto, which is situated on longitude 79 degrees, 20 minutes west and latitude 43 degrees, 40 minutes north at approximately 380 feet above sea level. The city lies on the north shore of Lake Ontario, the smallest of the North American Great Lakes (fresh water), open to ocean shipping via the St. Lawrence Seaway and fed from the local watershed and the Niagara River draining Lake Erie. Lake Ontario supports a variety of fish but owing to increasing pollution, fishing is no longer of com-

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mercial or sporting value. The annual rainfall has varied from 35.81" in 1945 to 19.74" in 1949; in 1959 it was 25.15". The maximum and minimum temperatures have varied from 94° F. on August 14, 1959, to minus 3° F. on January 5, 1959. The direction of the prevailing wind is usually northwest.

The growth of this city over the past 15 years has been spectacular, but this has been greatest on the western outskirts where this survey was conducted. The population of the Township of Etobicoke was 25,000 in 1945; in April 1960 when the sampling ceased, it was estimated at 145,000, a 500% increase, which clearly illustrated the degree of immigration and development that has taken place. Thus, it will be seen that any attempt to break down results in relation to a static population is impossible and this will have to be accomplished by other criteria.

Numerous authors have suggested that the portal of entry of the infection is the alimentary tract and that meat could be the medium,[12] but this has been questioned. The area under survey contains no abattoirs: the main source of meat supply is cattle from Ontario, although a small proportion comes from other parts of Canada. Frozen lamb is imported from New Zealand and canned meats from the United States and elsewhere. All fresh meat is inspected except for a very occasional local slaughter by a butcher. A survey is being undertaken at the time of writing to determine whether cattle population samples in Ontario have significant dye test titres as evidence of past or present infections.

There has been no indication from the study of the literature and reported case histories that toxoplasmosis is either a water-borne or a milk-borne disease, or in fact that it could be related to ineffective sanitation in the widest sense. The present survey area receives its water supply from Lake Ontario after treatment by the Metropolitan Toronto filter plants; its milk supply comes from dairy cattle within a hundred miles of the city, after pasteurization. The sewage disposal is carried out by municipal plants with subsequent aeration and emptying of the purified effluent into Lake Ontario. There are, however, numbers of dwellings with septic tank drainage and the drawbacks that these possess in an urbanized area.

The terrain has changed rapidly over recent years owing to urbanization and at the time of the survey consisted almost entirely of a fully developed and serviced living area, bounded on the east by the Humber River and on the west by the Etobicoke Creek, on the north by open farm land and the south by Lake Ontario. Through the centre, from the north to south, runs the Mimico Creek.

RESULTS

These have been separated into two components: (1) the findings of the epidemiological survey carried out by means of the toxoplasmin skin test and Sabin-Feldman dye test; and (2) the comparative study of the value to the dye test, complement fixation test and hemagglutination test, as indicators of past infection for use in surveys. The quality of the sample material and the method of collection have enabled us to define the incidence of previous infection with *Toxoplasma gondii* in the area under study and at the same time to evaluate certain social and environmental factors not previously recorded elsewhere. The criteria for significant positive reactions which have been outlined above have been rigidly adhered to.

TABLE I.—PERCENTAGE OF DYE AND SKIN TESTS POSITIVE BY AGE AND SEX

Age	Total tested	Dye test positive No.	Dye test positive %	Skin test positive No.	Skin test positive %
		Males			
1	9	—	—	—	—
5	23	1	4.3	1	4.3
10	40	8	20.0	6	15.0
20	45	10	22.2	9	20.0
30	47	16	34.0	12	25.5
40	40	14	35.0	7	17.5
50	60	25	41.7	18	30.0
60	32	15	46.9	5	16.1
70+	18	5	27.8	7	38.9
	314	94	30.0	65	20.8
		Females			
1	9	—	—	—	—
5	22	1	4.5	—	—
10	47	7	14.9	7	14.9
20	56	10	17.8	14	25.0
30	52	9	17.3	7	13.5
40	60	13	21.7	19	31.7
50	40	11	27.5	10	25.0
60	28	13	46.4	11	37.9
70+	22	8	36.4	9	40.9
	336	72	21.4	77	22.8
		Total			
1	18	—	—	—	—
5	45	2	4.4	1	2.2
10	87	15	17.2	13	14.9
20	101	20	19.8	23	22.8
30	99	25	25.2	19	19.2
40	100	27	27.0	26	26.0
50	100	36	36.0	28	28.0
60	60	28	46.7	16	26.7
70+	40	13	32.5	16	40.0
	650	166	25.5	142	21.8

The percentage of positive results by age and sex are recorded for the dye test and the skin test (Table I). The proportion of positive dye-test results is higher among males than among females (30.0%, compared with 21.4%) but this difference is not statistically significant. The difference in the male and female rates lies almost entirely in the wide age group 30-59; under the age of 30 and over 60 there is almost no difference between males and females in the percentage of positive dye tests. The percentage of positive skin tests, like the corresponding percentage of dye tests, increases with age, but there is almost no difference between males and females. Fig. 2 shows the percentage of positive results by age and sex for the two tests; here the general upward trend with increasing age is

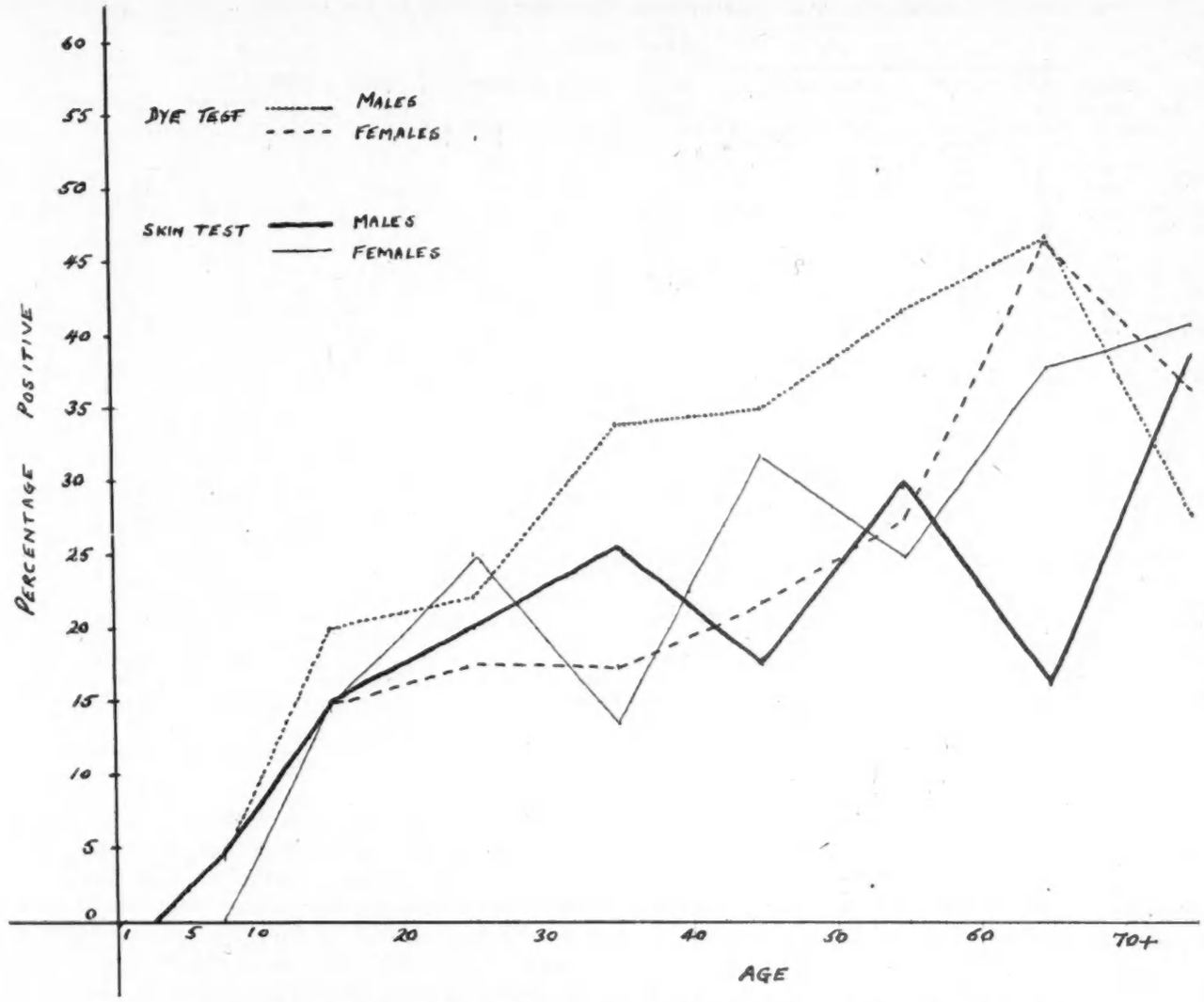

Fig. 2.—The percentage of positive dye and skin test reactors by age and sex: the general upward trend with increasing age is illustrated.

illustrated. The percentage of positive results found in patients aged 70 and over decreases sharply in the dye test, but not in the skin test.

The dye-test readings for the 166 patients with positive tests are presented by age and sex (Table II). Approximately three-quarters of all positive dye-test results are in titres less than 1/256 and there is no sex difference in this percentage. There is, however, a tendency for the younger patients with positive dye tests to have higher readings than the older patients. Of the 37 patients with positive dye test who are under 30 years of age in this study, 16 (43%) had readings of 1/256 or over, while only 18% of the 129 patients who are over 30 and had positive dye tests had readings of 1/256 or over. This difference is statistically significant and could indicate a relationship to the onset of infection with *Toxoplasma gondii* in the earlier years.

A rather poor correlation exists between the dye-test and the skin-test results. Of the 166 subjects with positive dye tests, 71 or 42% had a negative skin test. The proportion of persons with a positive dye test and a negative skin test is greatest, as might be expected, among those with lower dye-test readings: there were only 10 persons with negative skin tests and a dye-test result of 1/256 or over.

The 10 patients with a negative skin test and a dye-test reading of 1/256 or over do not seem to have much else in common (Table III). Five are male and five are female. Only two had any appreciable rise in temperature during their hospital stay that might conceivably have modified their skin sensitivity. Five are over 60 years of age, while four are under 20.

The discharge diagnoses are shown for the 650 patients included in the study, by sex, together with the number of positive dye-test results in each diagnostic group (Table IV). Because of the different age distribution in the diagnostic group and because the percentage of positive dye tests increases with age (Fig. 2), it was not possible to calculate cause specific rates. For example, the respiratory disease group, most of whom are children with chronic tonsillitis, would be expected to have a lower percentage of positive dye-test readings than the patients with malignant neoplasms. The expected numbers of positive cases are shown

TABLE II.—POSITIVE DYE TESTS (DYE TEST READING) BY AGE AND SEX

Age	Total tested	Both tests negative	Dye test reading												Skin test only positive
			1/16	1/32	1/64	1/128	Under 1/256	1/256	1/512	1/1024	1/2048	1/4096	1/256 and over	Total positive	
Males															
1-4	9	9	—	—	—	—	—	—	—	—	—	—	—	—	—
5-9	23	22	—	1	—	—	1	—	—	—	—	—	—	1	—
10-19	40	31	1(1)	—	1	1(1)	3(2)	2(1)	6	—	—	1	5(1)	8(3)	1
20-29	45	33	2(1)	2(1)	2	—	6(2)	2(1)	1	1	—	—	4(1)	10(3)	2
30-39	47	27	5(2)	3(2)	3(2)	3(1)	14(7)	—	2(1)	—	—	—	2(1)	16(8)	4
40-49	40	23	4(4)	2(2)	3(2)	3(2)	12(10)	1	—	1	—	—	2	14(10)	3
50-59	60	30	5(2)	4(3)	8(6)	6(1)	23(12)	2	—	—	—	—	2	25(12)	5
60-69	32	17	2(2)	5(3)	2(2)	1	10(7)	4(1)	1(1)	—	—	—	5(2)	15(9)	—
70+	18	10	—	1	2(1)	1	4(1)	1	—	—	—	—	1	5(1)	3
Total	314	202	19(12)	18(11)	21(13)	15(5)	73(14)	12(3)	6(2)	2	—	1	21(5)	94(46)	18
Females															
1-4	9	9	—	—	—	—	—	—	—	—	—	—	—	—	—
5-9	22	21	—	—	—	—	—	1(1)	—	—	—	—	1(1)	1(1)	—
10-19	47	38	—	1	—	3(1)	4(1)	3(1)	—	—	—	—	3(1)	7(2)	2
20-29	56	41	1	2(1)	2	2	7(1)	1	—	1	1	—	3	10(1)	5
30-39	52	41	2(1)	2	3(3)	—	7(4)	2	—	—	—	—	2	9(4)	2
40-49	60	38	2	4(2)	3(1)	—	9(3)	3	1	—	—	—	4	13(3)	9
50-59	40	24	5(4)	3(1)	1(1)	2	11(6)	—	—	—	—	—	—	11(6)	5
60-69	28	12	—	2	5(3)	2	9(3)	3(3)	1	—	—	—	4(3)	14(6)	3
70+	22	11	1(1)	3	3(1)	—	7(2)	—	—	—	1	—	1	8(2)	3
Total	336	235	11(6)	17(4)	17(9)	19(1)	54(20)	13(5)	2	1	2	—	18(5)	73(25)	29
Total	650	437	30(18)	35(15)	38(22)	24(6)	127(61)	25(8)	8(2)	3	2	1	39(10)	166(71)	47

Note: Figures in parentheses refer to cases with a positive dye test result but a negative skin test.

for each cause so that they can be compared with the observed number of positive cases: the expected numbers are calculated by applying the age and sex specific rates shown in Table I to the age and sex distributions of each cause group.

None of the differences between the observed and the expected numbers of cases were statistically significant, although there are several differences worth further investigation. The groups with more positive results than would be expected, if we assume that no differences exist between causes in the proportion of postive results, are those with allergic, endocrine, metabolic, nutritional, respiratory and genitourinary diseases (males only). Causes with fewer positive results than expected are diseases of the circulatory system and of the digestive system (females only).

Table V shows the cases with positive dye tests, tabulated according to discharge diagnoses. The proportion of dye-test readings 1/256 and over seems fairly high among patients who were treated for diseases of the respiratory system and for accidents, but this may reflect the fact that these diagnostic groups include a number of young patients who apparently tend to have higher dye-test readings. The proportion of positive skin tests in patients who have negative dye tests is high among those treated for circulatory diseases and again this may be due to the higher age group as illustrated by Fig. 1.

The number of positive dye tests in patients with an elevated temperature at some time during their stay in hospital is shown in Table VI, along with the corresponding dye-test results among patients

TABLE III.—PATIENTS WITH A NEGATIVE SKIN TEST RESULT AND A DYE TEST READING OF 1/256 OR OVER

Exp. No.	Discharge diagnosis	Age	Sex	Birthplace	Present location cypher	Number in household	Febrile
154	Perforated appendicitis	17	M	Toronto	D10	5	98.2-102.6
189	Hemorrhoids	37	M	Hamilton	F7	5	97.4- 99.6
493	Chest pain of undetermined cause—suspect hiatus hernia	23	M	England	G8	6	97.0-100.2
570	Mitral stenosis and insufficiency, secondary anemia	61	M	Stratford	D10	3	96.0- 99.4
651	Lacerations knee, forehead, fractured ribs	60	M	?	C11	2	97.0- 99.6
473	Chronic tonsillitis	6	F	Toronto	C10	5	99.0- 99.4
578	Chronic bronchitis	62	M	England	E8	2	96.8- 99.0
628	Cataract (R) eye	66	F	Russia	D5	3	96.4- 99.4
639	Deviated nasal septum	19	F	England	D8	4	97.4- 99.0
689	Diverticulum of duodenum Chronic rheumatic heart disease	67	F	England	B10	3	96.0- 99.4

TABLE IV.—OBSERVED AND EXPECTED NUMBERS OF POSITIVE DYE TESTS BY SEX AND DISCHARGE DIAGNOSIS

I.C.D.* number	Discharge diagnosis	Males			Females			Total		
		Total Tested	Positive tests		Total Tested	Positive tests		Total Tested	Positive tests	
			Actual	Expected		Actual	Expected		Actual	Expected
001-138	Infective and parasitic diseases	7	2	2.3	4	1	0.7	11	3	3.0
140-205	Malignant neoplasms	10	4	3.9	12	3	4.0	22	7	7.9
210-239	Benign and unspecified neoplasms	8	3	2.4	28	6	6.1	36	9	8.5
240-289	Allergic, endocrine system, etc.	5	3	1.8	15	6	3.8	20	9	5.6
290-299	Diseases of the blood, etc.	2	—	0.8	2	—	0.4	4	—	1.2
330-398	Diseases of the nervous system	6	1	1.8	9	3	2.0	15	4	3.8
400-468	Diseases of the circulatory system	47	14	17.1	42	10	12.0	89	24	29.1
470-527	Diseases of the respiratory system	32	6	4.4	39	7	4.3	71	13	8.7
530-587	Diseases of the digestive system	84	26	25.7	68	8	14.0	152	34	39.7
590-637	Diseases of the genitourinary system	22	12	7.9	58	13	12.2	80	25	20.1
640-689	Complications of pregnancy and childbirth	—	—	—	7	1	1.2	7	1	1.2
690-716	Diseases of the skin and cellular tissue	3	1	0.8	6	—	1.4	9	1	2.2
720-749	Diseases of the bones, etc.	30	10	9.7	16	5	3.6	46	15	13.3
750-759	Congenital malformations	6	—	1.1	2	—	0.4	8	—	1.5
780-795 300-326	Symptoms, ill-defined conditions	6	1	1.6	5	1	0.8	11	2	2.4
N800-N999	Accidents, poisonings, and violence	46	11	12.7	23	8	5.1	69	19	17.8
		314	94	94.0	336	72	72.0	650	166	166.0

*International Classification of Diseases.

with no temperature elevation or with a low-grade fever only. An oral temperature reading of 100° F. was arbitrarily chosen as an elevated temperature. There is no difference whatsoever in the proportions of cases with a positive dye-test result, so we assume that a moderate elevation of temperature has no significant effect on the dye-test results.

Table VII shows the number of patients who had family pets at home and designates the kind of pet. Of the 650 patients in the study, 292 or 44.9% had at least one animal at home. Dogs were the most popular family pet, followed by budgerigars (including tropical birds) and cats; 100 patients had more than one species of animal pet. Dogs were chosen as the most important animal, cats ranking second. Thus, for example, a patient with both a dog and a cat would be shown in the column "dog alone and with other", while a pa-

TABLE V.—POSITIVE DYE TEST RESULTS BY DISCHARGE DIAGNOSIS

Diagnosis	Total tested	Both tests negative	Dye test positive		Skin test positive only
			Under 1/256	1/256 and over	
001-138	11	8	3	—	—
140-205	22	14	6	1	1
210-239	36	26	8	1	1
240-289	20	11	8	1	—
290-299	4	2	—	—	2
330-398	15	10	3	1	1
400-468	89	50	18	6	15
470-527	71	57	6	7	1
530-587	152	110	27	7	8
590-637	80	49	21	4	6
640-689	7	5	1	—	1
690-716	9	7	—	1	1
720-749	46	25	12	3	6
750-759	8	8	—	—	—
780-795 300-326	11	9	1	1	—
N800-N999	69	46	13	6	4
Total	650	437	127	39	47

TABLE VI.—PERCENTAGE OF DYE TESTS POSITIVE BY AGE, SEX AND TEMPERATURE DURING HOSPITAL STAY

Age	Temperature range under 100°F.			Temperature range 100°F. and over		
	Total tested	Positive tests		Total tested	Positive tests	
		Number	%		Number	%
			Males			
1- 4	2	—	—	7	—	—
5- 9	7	—	—	16	1	6.2
10-19	19	2	10.5	21	6	28.6
20-29	19	4	21.0	26	6	23.1
30-39	22	8	36.4	25	8	32.0
40-49	19	5	26.3	21	9	42.8
50-59	29	14	48.3	31	11	35.5
60-69	13	6	46.2	19	9	47.4
70+	10	4	40.0	8	1	12.5
Total	140	43	30.7	174	51	29.3
Age			Females			
1- 4	1	—	—	8	—	—
5- 9	9	1	11.1	13	—	—
10-19	27	4	14.8	20	3	15.0
20-29	40	6	15.0	16	4	25.0
30-39	34	6	17.6	18	3	16.7
40-49	32	8	25.0	28	5	17.8
50-59	15	4	26.7	25	7	28.0
60-69	14	7	50.0	14	6	42.8
70+	14	4	28.6	8	4	50.0
Total	186	40	21.5	150	32	21.3

TABLE VII.—NUMBER OF PATIENTS TESTED AND NUMBER OF POSITIVE DYE TESTS, BY AGE AND TYPE OF HOUSEHOLD PET

			Household pets													
	No household pets		*Dog alone and with other*		*Cat alone and with other*		*Canary alone*		*Budgie* alone and with other*		*Goldfish and tropical fish*		*All other†*		*Total*	
Age			*No.*	*Pos.*	*No.*	*Pos.*	*No.*	*Pos.*	*No.*	*Pos.*	*No.*	*Pos.*	*No.*	*Pos.*	*No.*	*Pos.*
1- 4	9	—	3	—	—	—	—	—	2	—	3	—	1	—	9	—
5- 9	26	1	5	1	2	—	—	—	4	—	3	—	5	—	19	1
10-19	41	9	20	5	10	—	1	—	7	—	5	1	3	—	46	6
20-29	66	14	14	1	5	1	1	—	10	3	5	1	—	—	35	6
30-39	55	8	18	6	9	4	1	—	8	3	6	4	2	—	44	17
40-49	50	16	24	4	9	2	1	1	13	3	2	—	1	1	50	11
50-59	59	19	15	7	8	3	4	1	11	4	2	1	1	1	41	17
60-69	29	12	14	9	7	3	4	1	6	3	—	—	—	—	31	16
70+	23	8	10	3	1	—	2	1	4	1	—	—	—	—	17	5
Total	358	87	123	36	51	13	14	4	65	17	26	7	13	2	292	79
Per cent positive	24.3		29.3		25.5		28.6		26.2		26.9		15.4		27.0	

*Includes "tropical birds" and "bird" unspecified.
†Includes hamsters, rabbits, turtles, pigeons, guinea pigs.

tient with a budgerigar, a cat and a goldfish would be listed under "cat alone and with other".

There is little difference in the age distributions of patients with pets and those without pets, so the percentage of positive dye tests, all ages combined, is computed for each column. There is a slight tendency for patients with pets to have a higher number of positive results, but this difference is very small and is probably due to chance variation alone.

Robertson[18] has summarized the views reported to date concerning the relation of dye-test levels to the onset of infection and has concluded "that after infection, titres rise over a period of a few months to very high levels—of the order of 1/10,000—remain there for a short time and then fall. The fall is rapid at first and then becomes much slower, low titres persisting for many years. The rate of rise and fall is very variable. (The former may increase tenfold within a few days.[17]) Titres from 1/128 to 1/1024 might be expected 11 months after infection, while four years after infection, they would be between 1/16 and 1/256." The period of residence in the survey area of the patients in this survey has been assessed for those with titres 1/128 or more (Table VIII), as this might be expected under the above criterion to indicate those individuals who have developed the infection while living in the survey area although not necessarily being infected from a source within the area.

TABLE VIII.—NUMBER OF DYE TESTS 1/128 OR HIGHER RELATED TO PLACE OF RESIDENCE OVER THE LAST FIVE YEARS

	Total cases tested	**Cases with dye test 1/128 or higher*	*Residents of total survey area*	*Residents of Etobicoke*	*Residents outside Etobicoke but in survey area*	**Residents outside survey area*
Moved within Greater Toronto only in past 5 years			46 (75.4%)	36 (85.7%)	10 (52.6%)	—
Did not move in past 6 years			7 (11.5%)	—	5 (26.3%)	2 (10.5%)
Moved from elsewhere in Ontario			3 (5.0%)	1 (2.4%)	2 (10.5%)	
Moved from elsewhere in Canada			2 (3.2%)	2 (4.8%)	—	—
Moved from outside Canada			3 (8.2%)	3 (7.1%)	2 (10.5%)	—
Total	650	*63	61	42	19	2

*1 resident of Buffalo, N.Y.; 1 resident of Dufferin County.

Of the 63 cases with dye-test titres greater than 1/128, 61 or 96.8% were resident in the survey area at the time of testing; one subject resided in Dufferin County and one in Buffalo, New York. Of the 61 cases, 46 or 75.4% had lived within a radius of 20 miles from the centre of Toronto for at least five years. Therefore, of the 650 cases tested in the survey 46 or 7% could conceivably have developed their infection while living in the survey area.

In Table IX are shown the actual numbers of positive dye tests according to the racial origin of

TABLE IX.—ACTUAL AND EXPECTED NUMBERS OF POSITIVE DYE TEST READINGS BY RACIAL ORIGIN

	Dye test reading under 1/256		*Dye test reading 1/256 and over*		*Total*	
Racial origin	*Actual*	*Expected*	*A*	*E*	*A*	*E*
British	67	68	20	20	87	88
Canadian	19	25	9	10	28	35
French	4	4	—	1	4	5
Italian	9	6	3	2	12	8
German	5	4	1	1	6	5
Polish	6	5	—	1	6	6
Ukrainian	3	4	3	1	6	5
Dutch	1	1	1	—	2	1
Scandinavian and Baltic countries	7	5	—	1	7	6
Other	6	5	2	2	8	7
Total	127	127	39	39	166	166

TABLE X.—637 PATIENTS ON WHOM ALL FOUR TESTS WERE CARRIED OUT.

Age	Total tested	Skin test positive		Complement fixation test positive		Hemagglutination test positive		Dye test positive	
		No.	%	No.	%	No.	%	No.	%
					Males				
1- 4	9	—	—	—	—	—	—	—	—
5- 9	23	1	4.3	—	—	—	—	1	4.3
10-19	40	6	15.0	3	7.5	4	10.0	8	20.0
20-29	42	7	16.7	1	2.4	4	9.5	9	21.4
30-39	46	11	23.9	2	4.3	2	4.3	15	32.6
40-49	39	7	17.9	2	5.1	6	15.4	14	35.9
50-59	60	18	30.0	1	1.7	3	5.0	25	41.7
60+	50	12	24.0	3	6.0	3	6.0	20	40.0
	309	62	20.1	12	3.9	22	7.1	92	29.8
					Females				
1- 4	9	—	—	—	—	—	—	—	—
5- 9	21	—	—	—	—	1	4.8	1	4.8
10-19	47	7	14.9	2	4.2	2	4.2	7	14.9
20-29	54	12	22.2	4	7.4	6	11.1	9	16.7
30-39	51	7	13.7	1	2.0	3	5.9	9	17.6
40-49	60	19	31.7	3	5.0	7	11.7	13	21.7
50-59	39	10	25.6	1	2.6	4	10.2	11	28.2
60+	47	19	40.4	2	4.2	3	6.4	19	40.4
	328	74	22.6	13	4.0	26	7.9	69	21.0
					Total				
1- 4	18	—	—	—	—	—	—	—	—
5- 9	44	1	2.3	—	—	1	2.3	2	4.6
10-19	87	13	14.9	5	5.7	6	6.9	15	17.2
20-29	96	19	19.8	5	5.2	10	10.4	18	18.8
30-39	97	18	18.6	3	3.1	5	5.2	24	24.7
40-49	99	26	26.3	5	5.0	13	13.1	27	27.3
50-59	99	28	28.3	2	2.0	7	7.1	36	36.4
60+	97	31	32.0	5	5.2	6	6.2	39	40.2
Total	637	136	21.3	25	3.9	48	7.5	161	25.3

the subjects concerned. The only two findings that emerge, and these are of no more than borderline significance, are firstly, that Canadians have fewer positive tests than expected, and secondly that Italians have more than expected. There is something unusual in this latter observation which may be related to social and other factors and could be pursued in future studies. However, the actual numbers themselves are too small for accurate statistical breakdown.

Table X shows that the proportion of positive dye tests and positive skin tests increases with age, but there is no evidence that age has any influence on the proportion of patients with positive hemagglutination and complement fixation tests. Males have a higher number of positive dye tests than do females, and this difference lies entirely in the age group 20-60; under 20 and over 60 years of age there is no difference between the sexes in the percentage of positive dye tests. No significant differences were found between males and females in the percentage of positive skin, complement fixation, and hemagglutination tests, and there was no significant correlation between these tests and the dye test.

DISCUSSION

The specificity of the Sabin-Feldman dye test has been questioned many times since its introduction. Nevertheless, it has withstood such criticism despite the suspicion of some cross-antigenicity with Sarcocystis. Human infection with the latter is rare, but not unknown[19-21] and thus the possibility of cross-reaction, while improbable, is not impossible. Kimball *et al.*[11] have discussed this observation in relation to the possible development of false positive reactions among persons eating raw beef: they were unable to demonstrate unequivocally this association despite the fact that the raw beef consumed was derived from Sarcocystis-infected cattle. Thus, for this sampling, we are justified in assuming that a positive dye test of required titre is an indication that an individual has at some time become infected with *Toxoplasma gondii*. That a significant proportion (25.5%) of the population of an urban area in southern Ontario has been so infected has been amply demonstrated by this survey (Table I). Moreover, 46 of 650, or 7%, of a sample population may have contracted the infection while living in the survey area (Table VIII). That active human infection with *Toxoplasma gondii* does occur within Ontario, we know from unpublished studies utilizing histological and cultural

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methods,[4] and have suspected from a published survey.[3] Furthermore, there is increasing evidence that a proportion of cases of chorioretinitis in the Toronto area, both in infancy and in later life, are caused by *Toxoplasma gondii* infection or products of that infection, as implied by the results of specific dye tests and complement fixation tests carried out in our laboratories.

We cannot dispute Feldman's[7] contention that the value of the skin test is doubtful and do not feel that it is of any value for screening purposes, having only 60% efficiency when related to the dye test, and on 10 occasions being negative when a dye-test titre was 1/256 or more. Furthermore, 47 positive skin-test reactors had negative dye tests; we cannot account for the significance of this finding. On the other hand we have been impressed with two findings: firstly, the predominance of certain national or racial groups among the positive dye-test reactors, secondly, the distribution of these reactors within comparatively narrow boundaries in the survey area (Fig. 2). Both could certainly be related to a number of factors, but it might be that the two are interrelated as has been suggested by Kimball and others,[11] who found that the geographical significance was greater than the racial. We have demonstrated an unusually heavy concentration of positive reactors within even narrower limits, a finding which will form the subject of future investigation; we can only hazard a guess that the distribution of the different nationalities may in part account for this. It is beyond the scope of this investigation to inquire deeply into these factors, but undoubtedly some interesting information could result from the further breakdown of these two elements in the present survey and will, it is hoped, be pursued particularly in relation to food habits and to personal and environmental hygiene. We have not, however, been able to demonstrate any significant correlation between positive reactors and the possession of pets: this by itself is not unexpected, particularly as we have no knowledge of the dye-test reactions of the animals concerned. Actually, at the present time, it is considered that if both humans and pets are infected they may well have been infected from a common source rather than that either should have infected the other.

During the survey we obtained 63 dye-test reactors with titres greater than 1/128, an incidence of 9.7% of those tested and 38% of those with positive dye tests. Assuming that a titre of 1/128 may be evidence of infection developed within the past year,[18] this suggests that a proportion of people are actually undergoing infection at any one time and that some may develop overt if unrecognized disease and others subclinical infection. This is the challenge which is being accepted and a survey of domestic animals is under way in Ontario. It is hoped shortly to initiate a survey of the wild fauna in view of numerous reports of the incidental finding of *Toxoplasma gondii*, particularly in small rodents.[23, 24] In a previous paper,[2] the possibility that small animals "coming into constant proximity to man" either by themselves or by their ectoparasites could be the vector of the disease was suggested. The prevalence of the North American grey squirrel (*Sciuris carolensis*) in newly developed suburban areas has been noted, and it is suspected that this rodent might bear responsibility in spreading a number of, at present, undefined diseases. There has recently been some support for this thinking in the report[25] of the finding of *Toxoplasma gondii* in a grey squirrel (*Sciuris grisues*) in California which had been seen to be behaving in an abnormal manner and had bitten a child. The animal was impounded and died in a coma the next day, but no evidence of rabies was found.

In conclusion, we have not been able to demonstrate a significant advantage in either the complement fixation test or the hemagglutination test over the dye test as indicators of existing levels of Toxoplasma antibody in a sample population. The fact that each test probably measures a different antibody is considered very probable. We mention once again the possibility that the dye test is not entirely specific, and putting all these facts together it will be seen that survey work concerning this interesting infection has still to undergo considerable development; and until equally reliable and repeatable methods of isolating the organism from overt and occult cases of toxoplasmosis are found, reliance will have to continue to be placed upon the dye test, which, even if not entirely specific, has up till now been shown to be the only satisfactory and reproducible test available.

SUMMARY

A survey of a sample population in Ontario has been carried out to determine the levels of Toxoplasma antibody as measured by skin, complement fixation, hemagglutination and Sabin-Feldman dye tests.

Significant levels of cytoplasm-modifying antibody have been demonstrated (25.5% of a sample population) by the dye test, but these have not been reproducible by the other tests and no significant correlation between them exists, when used for survey purposes. The implications of the presence of Toxoplasma infection in a community have been discussed and suggestions for further investigations have been advanced.

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REFERENCES

1. HULLAND, T. J.: *J. Am. Vet. M. A.*, **128**: 74, 1956.
2. FFRENCH, G. E.: *Canad. M. A. J.*, **80**: 910, 1959.
3. HARPER, D. W., ORMSBY, H. L. AND COCKERAM, A.: *Ibid.*, **79**: 25, 1958.
4. CROZIER, D. N.: Personal communication, 1957.
5. PRIDHAM, T. J. AND BELCHER, J.: *Canad. J. Comp. Med.*, **22**: 99, 1958.
6. FELDMAN, H. A. AND MILLER, L. T.: *Am. J. Hyg.*, **64**: 320, 1956.
7. FELDMAN, H. A.: *Pediatrics*, **22**: 559, 1958.
8. BEVERLEY, J. K. A. AND BEATTIE, C. P.: *Lancet*, **2**: 379, 1958.
9. VON ZEIPEL, G. AND LINDER, L. A.: *Acta path. et microbiol. scandinav.*, **29**: 229, 1951.
10. CATHIE, I. A. B. AND DUDGEON, J. A.: *Great Ormond St. J.*, **51**: 13, June 1953.
11. KIMBALL, A. C. *et al.*: *Am. J. Hyg.*, **71**: 93, 1960.
12. JACOBS, L., COOK, M. K. AND NEUMANN, E.: *J. Parasitol.*, **40**: 701, 1954.
13. GRÖNROOS, P.: *Ann. med. exper. et biol. Fenniae* (supp. II), **33**: 1-113, 1955.
14. SABIN, A. B. AND FELDMAN, H. A.: *Science*, **108**: 660, 1948.
15. LABZOFFSKY, N. A. AND FISCHER, J. B.: *Canad. J. Microbiol.*, **1**: 520, 1955.
16. JACOBS, L. AND LUNDE, M. N.: *J. Parasitol.*, **43**: 308, 1957.
17. SIIM, J. C.: Personal communication, 1960.
18. ROBERTSON, J. S.: *Brit. M. J.*, **2**: 91, 1960.
19. HEWITT, J. A.: *J. Path. & Bact.*, **36**: 133, 1933.
20. GILMORE, H. R., JR., KEAN, B. H. AND POSEY, F. M.: *Am. J. Trop. Med.*, **22**: 121, 1942.
21. MCGILL, R. J. AND GOODBODY, R. A.: *Brit. M. J.*, **2**: 333, 1957.
22. SABIN, A. B.: *Am. J. Ophth.*, **41**: 600, 1956.
23. COLES, A. C.: *Parasitology*, **7**: 17, 1914.
24. SIMITCH, T., PETROVITCH, Z. AND BORDJOCHKI, A.: *Arch. inst. pasteur Algérie*, **34**: 93, 1956.
25. SOAVE, O. A. AND LENNETTE, E. H.: *J. Lab. & Clin. Med.*, **53**: 163, 1959.

THE METABOLISM OF THE VOLATILE AMINES*
I. THE AMMONIA CONTENT OF BLOOD

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IN RECENT YEARS there has been a renewed interest shown in the role of ammonia in certain clinical disease states. In 1893 workers in Pavlov's[1] laboratory described a syndrome called meat-intoxication (Fleischvergiftung) which was produced by the forced feeding of meat to Eck-fistula dogs, and which was attributed to the nitrogen content of meat. Several conflicting papers, particularly by Van Caulaert and Deviller,[2] Kirk,[3] and Monguió and Krause,[4] were published about 1930 discussing the decreased tolerance of the diseased liver to ammonium salts. Since 1952 an extensive series of articles[5-8] has described and debated the relationship between blood ammonia levels and acute hepatic encephalopathy. It has become evident that the ammonia content of blood has some inconstant relationship to neurological disorders, particularly in patients with liver disease.

Many techniques have been used in the measurement of the minute quantity of ammonia present in blood, although they are all individual modifications of two basically similar methods. Conway and Byrne[9] in 1933 described a microdiffusion technique for measuring the volatile amines present in aqueous solutions which involved the back-titration of the absorbing acid by dilute barium hydroxide. This method was soon adapted to measure the ammonia content of blood.[10] In 1951, Seligson and Seligson[11] introduced their method which involved the estimation of the diffused ammonia by a modified Nessler's reagent.

Because of the fact that both techniques have many technical disadvantages, individual workers in this field have adapted one or other method to suit their particular needs. As a result, so many minor modifications have been described in the literature that it is impossible to compare the blood ammonia levels obtained in different laboratories, and at times even in the same laboratory.

The purpose of this paper is to suggest a means whereby the results of the various techniques can be standardized and to present evidence that the ammonia content of blood, as determined by these techniques, is made up of two components. The technique used in measuring the blood ammonia nitrogen levels is a personal modification of that suggested by Conway.[12] It is described in some detail because there are several features which facilitate certain aspects of the test and which have not been previously clarified. Although the one method was used exclusively throughout this study, the conclusions reached are applicable to all techniques in current use.

MATERIALS

The reagents used in this test include saturated potassium carbonate solution, 0.0002 N hydrochloric acid and approximately 0.001 N barium hydroxide. The potassium carbonate was boiled for 10 minutes to free it from traces of ammonia and was then stored in a plastic bottle. Other alkali solutions such as potassium metaborate or potassium bicarbonate were not used.

Distilled water to a final volume of 500 ml. was added to a solution of 10 ml. of 0.01 N hydrochloric acid prepared from constant boiling-point stock, 100 ml. of absolute alcohol and 5 ml. of 0.08% methyl-red–0.02% methylene-blue indicator. Care was taken that the distilled water was both ammonia and carbon-dioxide free by redistilling it in the presence of barium hydroxide. Small amounts of carbonic acid were found to interfere with the test.

No effort was made to prepare a standard solution of barium hydroxide, as it was found that the very dilute solutions required would vary in concentration from day to day. A saturated solution which contained about 10% barium hydroxide at

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room temperature was diluted to about 0.001 N and stored in a wax-sealed reservoir. Small amounts were siphoned out periodically to refill the storage chamber attached to the microburette. This solution was standardized by titrating it against 1-ml. aliquots of the 0.0002 N hydrochloric acid several times during every series of determinations. The absorption of carbon dioxide explained why the dilute barium hydroxide solution occasionally decreased in strength, but no reason could be found to explain why it often increased.

Plastic diffusion dishes of the pattern described by Conway and Byrne[9] were used, as they were found to be superior to the accepted glass and porcelain dishes in many respects. They were almost unbreakable, easy to clean and relatively inexpensive. They could be used repeatedly despite the manufacturer's recommendation that they be discarded after one test. The lids had a flange around the periphery so that it was necessary only to brush on a thin layer of mineral oil in order to obtain an airtight seal instead of using petrolatum jelly or other solid fixatives. The oiled dishes were stored upside down to prevent any spattering of the mineral oil on to the diffusion surface. After use, the dishes were soaked in running water, washed in hot soapy water either by hand or by machine, and then acid-washed in 0.02 N sulfuric acid. After several rinsings in distilled water they were left to drain and evaporate dry. The pipettes were left in cleaning acid for several hours before being rinsed repeatedly with distilled water.

TECHNIQUE

The blood was drawn from either an antecubital vein with a tourniquet in place or from the femoral vein into a 10-ml. syringe containing about 0.15 ml. of 1 in 1000 heparin solution. Since this amount of heparin contained only about 0.15 μg. of ammonia nitrogen and was diluted with 10 ml. blood, its ammonia content was ignored. The blood was then transferred to a clean dry test tube and no effort was made to maintain either sterile or anaerobic conditions. This blood was added to the dishes as soon as convenient, usually within 10 minutes of shedding, although occasionally 30 to 40 minutes elapsed before all of the bloods were drawn and all of the dishes were set up.

The dishes were not always prepared ahead of time, as it took only about five minutes to prepare a set of 10 dishes. One ml. of 0.0002 N hydrochloric acid was accurately pipetted into the inner chamber and the dish rotated so that the entire surface was covered, and then approximately 1 ml. of the saturated potassium carbonate was quickly pipetted into one side of the outer chamber. After all of the dishes had been prepared, 1-ml. samples of blood were pipetted into the other side of the outer chamber of each dish, using an Ostwald blow-out pipette. The lids were then replaced and an airtight seal was ensured by lifting the dishes by their lids.

The blood and alkali were mixed by a gentle rotary motion for a timed period of 15 seconds and the dishes were then left on the bench top at room temperature, out of drafts and direct sunlight. The diffusion time was measured from the time the dishes were mixed until the lids were removed, as removal of the lids was equivalent to terminating the reaction. The acid remaining unneutralized in the inner chamber was titrated as soon as possible with the dilute barium hydroxide solution, using a Rehburg microburette. The end-point was taken as the complete disappearance of the reddish colour, at a pH of about 5.5.

The amount of acid neutralized by the ammonia was taken to be the difference between the titration values of the blanks and of the samples. Since 1 ml. of 0.0002 N hydrochloric acid is neutralized by 2.8 micrograms (μg.) of ammonia nitrogen, the amount of ammonia nitrogen present in the sample was calculated by multiplying 2.8 by the difference of the titrations and dividing by the blank titration value. The results were expressed as μg. of ammonia nitrogen per ml. of the material being analyzed. Whenever possible the titrations were performed in duplicate or triplicate, but on several time series only one titration could be done at each time.

The results reported here are those obtained from the bloods of normal people working in the laboratory as well as from many patients with various diseases in the Toronto General Hospital. All of the determinations were performed by the author.

RESULTS

The Diffusion of Ammonia from Standard Solutions

The relationship between the diffusion time and the per cent recovery from standard solutions of ammonium sulfate was constant and did not depend upon the original concentration of ammonia nitrogen in the standard in the range of 0.2 to 2.0 μg. per ml. The diffusion curve closely followed the algebraic expression $x = a\,(1 - e^{-0.055\,t})$, where "$a$" is the amount of ammonia nitrogen initially present in the standard solution and "x" is the amount of ammonia nitrogen measured in the diffusion time "t". The experimental curve deviated from the theoretical by a small exponential or sinusoidal factor which was related to the diffusion of ammonia through the depth of the liquid in the outer chamber.

It was impractical to allow the dishes to diffuse for the 80 minutes required for 99% recovery, as ammonia is produced by the action of strong alkali on blood, as will be discussed later. Accordingly a diffusion time of 20 minutes was employed in all determinations, since it corresponded to the recovery of 67% of the ammonia contained in the standard solutions. The factor which corrected for this incomplete diffusion was not applied to the results of the ammonia determinations done on blood and blood components. Other workers have

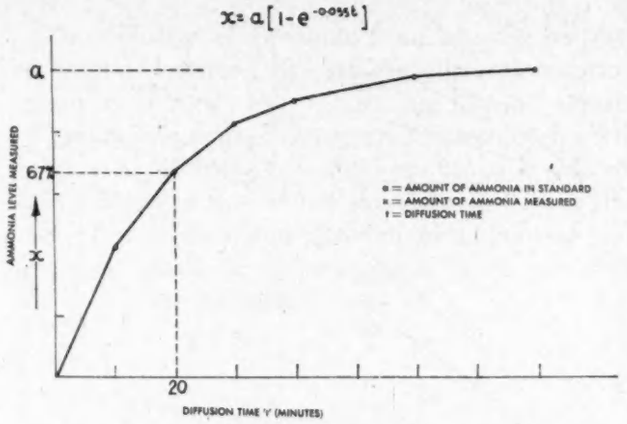

Fig. 1.—The effect of varying the diffusion time on the recovery of ammonia from standard solutions of ammonium sulfate containing 0.2 to 2 μg. NH_3-N per ml.

recommended diffusion times of 10,[13] 15[6] and 60[5] minutes, depending on the physical characteristics of their vessels and the per cent recovery desired.

The Diffusion of Ammonia from Blood

When blood is used in place of the standard ammonia-containing solutions, a different type of diffusion curve is obtained (Fig. 2). If blood drawn from a healthy human is set up immediately after shedding, a straight line relationship is obtained between the amount of ammonia diffused and the length of the diffusion period. Since this straight line can be extrapolated back through the origin, the algebraic expression for it is $x = bt$ where "x" is the amount of ammonia nitrogen measured in the diffusion time "t", and "b", the slope of the line, is the rate of new ammonia formation per unit time. This linear relationship persists for diffusion times of up to two hours.

The rate of new ammonia formation varies from person to person but appears to remain constant for each individual on repeated testing. It has a range of about 0.010 to 0.040 μg. per ml. of blood per minute in healthy people. It is quite apparent that the time allowed for diffusion is a very important factor in determining the blood ammonia

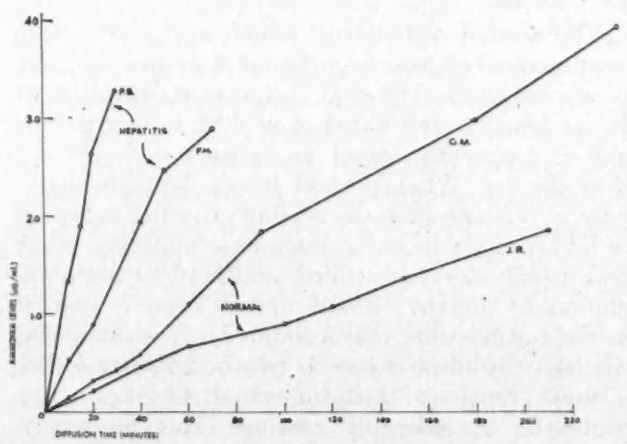

Fig. 2.—The effect of varying the diffusion time on the recovery of ammonia from the blood of persons with no recognizable liver disease and of some patients with acute hepatitis.

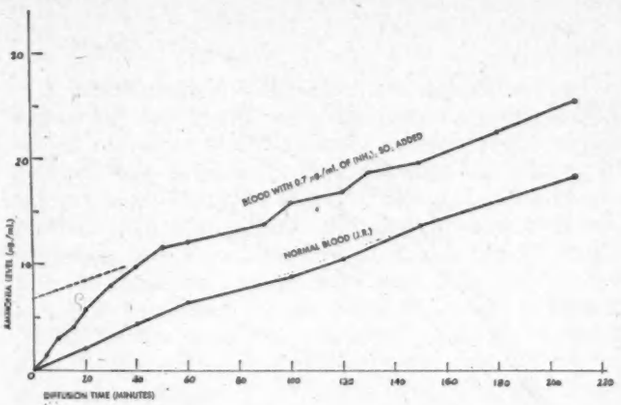

Fig. 3.—The effect of varying the diffusion time on the recovery of ammonia when ammonium sulfate is added to the blood of a healthy person.

nitrogen levels, as a diffusion time of 40 minutes will give exactly twice the level obtained in 20 minutes, and four times that when 10 minutes is employed as the diffusion time.

A composite type of curve is obtained if a small amount of standard ammonia solution is added to fresh whole blood from a healthy person before

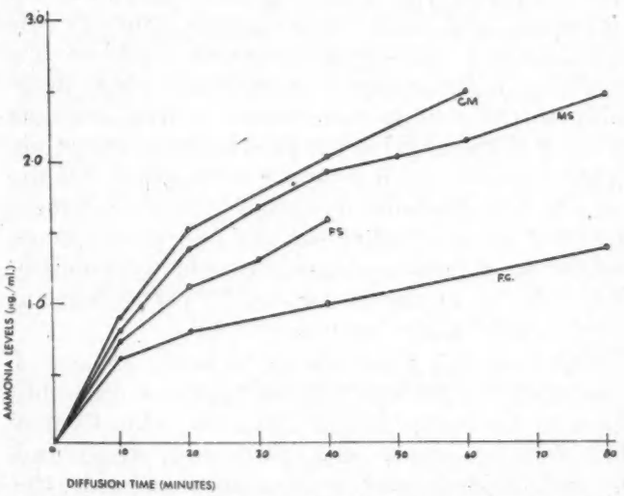

Fig. 4.—The effect of varying the diffusion time on the recovery of ammonia from the bloods of many patients with chronic liver disease.

the ammonia levels are determined (Fig. 3). Usually 0.1 ml. of an ammonium sulfate solution containing 70 μg. of ammonia nitrogen per ml. was added to 10 ml. blood. This amount of solution was sufficient to increase the ammonia content of blood by about 0.7 μg. per ml. and yet was small enough to obviate the problems of hemolysis and dilution. This curve, the sum of the two previous curves, closely follows the algebraic expression $x = a(1 - e^{-0.055t}) + bt$, where the symbols have the same meanings as before.

The exponential factor, which is very important over the first 30 minutes, rapidly decreases in effect until the line becomes linear after about 60 minutes and follows the expression $x = a + bt$. It is easy to estimate "a", the amount of ammonia nitrogen added to blood, by extrapolating the linear segment

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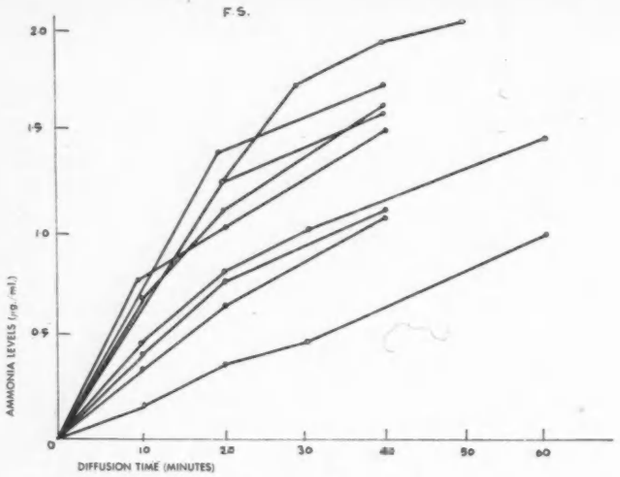

Fig. 5.—The variability of the ammonia diffusion curves of bloods drawn at different times from a patient suffering from alcoholic cirrhosis complicated by recurrent bouts of acute hepatic encephalopathy.

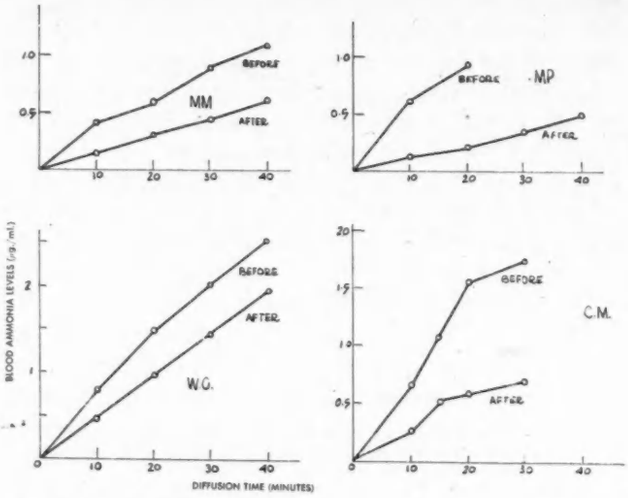

Fig. 7.—The effect of treatment on the ammonia diffusion curves of four patients with acute hepatic encephalopathy associated with gastrointestinal bleeding.

back and reading off the ammonia level at zero time. The rate of new ammonia formation can be found by measuring the slope of this linear portion.

The ammonia diffusion curves of blood drawn from patients with chronic liver disease resemble the composite type of curve with the mixture of exponential and linear time factors (Fig. 4). By extrapolating the linear segment back to the ordinate, a figure can be determined which probably corresponds to the amount of free ammonia present in the blood at the time the test was set up. The slope of the line which corresponds to the rate of new ammonia formation appears to remain constant for each individual, and may have a range similar to the range in normal people. Occasionally this rate is markedly increased, particularly in people with acute hepatic necrosis.

The level that may correspond to the amount of free ammonia present in blood varied considerably even in the same patient (Fig. 5). This level is increased by certain foods, particularly meats, and by certain drugs, such as ammonium chloride, the barbiturates and the carbonic acid anhydrase inhibitors. It is almost always this fraction of the blood ammonia which is increased in those patients who have high blood ammonia levels and are suffering from acute hepatic encephalopathy. After therapy with intravenous arginine-glutamate this fraction was either eliminated or considerably reduced in many patients (Figs. 6 and 7). This will be discussed in detail elsewhere.

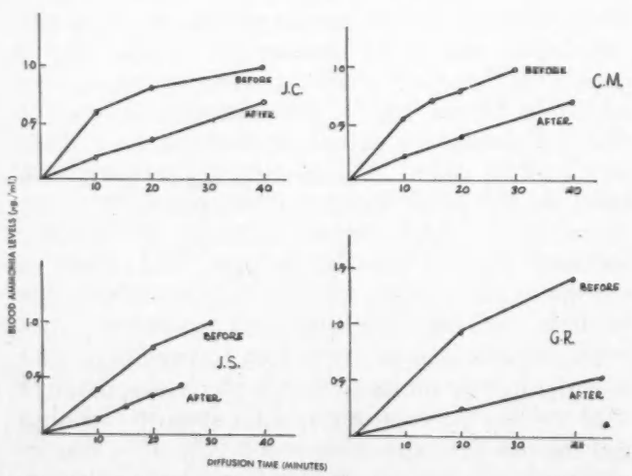

Fig. 6.—The effect of treatment on the ammonia diffusion curves of four patients with acute hepatic encephalopathy not associated with gastrointestinal bleeding.

DISCUSSION

The nature of the ammonia presumed to be present in blood has never been fully understood. It seems evident from this work that there are two components, one of which is invariably present and the other is found only in certain abnormal conditions. The first component is ammonia which is formed at a constant rate by the action of a strong alkali when mixed with human blood. The identity of the precursors of this fraction of the blood ammonia has not been established, although it has been considered that adenosine, adenylic acid and glutamine are involved. The rate of new ammonia nitrogen production has been found to vary from 0.010 to 0.040 μg. per ml. of blood per minute, both in normal people and in patients with liver disease.

The second component, which appears to be a combination of free ammonia and ammonium ion, is present in the blood at the time of shedding. It is not found in the blood of healthy fasting people and is frequently found in patients with chronic liver disease. When present it can fluctuate markedly in concentration, increasing after the ingestion of high-protein foods or ammonia-containing drugs and usually decreasing after antibiotic or arginine-glutamate therapy. Blood drawn from a patient in the fasting state may contain no free ammonia, whereas that drawn one to two hours after either a meat meal or gastrointestinal bleeding may contain a considerable amount. This may help to explain why some workers claim that there is free ammonia present in blood, while others deny its existence.

The diffusion of ammonia from blood using the technique described follows the algebraic expression $x = a\,(1 - e^{-0.055\,t}) + bt$ (see Fig. 8), where "x" is the amount of ammonia nitrogen measured in time "t", "a" is the free ammonia nitrogen present in the blood at the time of shedding and "b" is the rate of new ammonia nitrogen formation by the action of alkali. In normal people "a" is zero and the expression becomes $x = bt$.

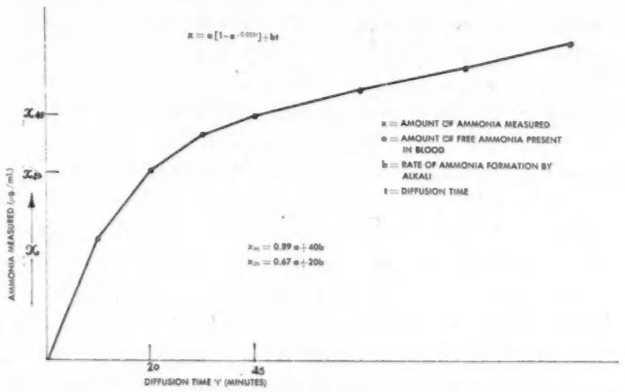
x = AMOUNT OF AMMONIA MEASURED
a = AMOUNT OF FREE AMMONIA PRESENT IN BLOOD
b = RATE OF AMMONIA FORMATION BY ALKALI
t = DIFFUSION TIME
AMMONIA MEASURED (c.c. ml.)
DIFFUSION TIME 't' (MINUTES)
20
45

Fig. 8.—A method of distinguishing between and measuring the two factors which constitute the blood ammonia level.

One can solve for "a" and "b" either by plotting a diffusion curve and extrapolating the linear segment, or by measuring "x" at two convenient times. If 20 and 40 minutes are used as the two diffusion periods the equation now becomes:

$$x_{20} = 0.67\,a + 20\,b$$
$$x_{40} = 0.89\,a + 40\,b.$$

It is then quite easy to calculate both the amount of free ammonia present in the blood and the rate of new ammonia formation by alkali. If each determination is done in triplicate, only 6 ml. of blood is required.

The general formula $x = a\,(1 - e^{-Kt}) + bt$ can be applied to any modification of the Conway technique. The value of the diffusion constant "K", which can be calculated from the diffusion curves of standard solutions of ammonia salts, depends on a great many factors, including the dimensions of the diffusion vessel, the room temperature, the amount of shaking and the volume, depth and surface area of the liquid in the outer chamber. Although this value of "K" is not precise, both because the diffusion of ammonia from blood takes place at a slower rate than that from aqueous solutions and because the rate of diffusion of the ammonia through the liquid is ignored, it is sufficiently accurate for the purposes of this test. Jacquez, Jeltsch and Hood[14] have suggested a similar formula which can be applied to the Seligson technique.

SUMMARY

A modification of the Conway technique used in measuring the blood ammonia levels is described in which re-usable plastic dishes are used and few precautions are employed when drawing the blood. By using various diffusion times, a diffusion curve can be plotted from which both the rate of new ammonia formation and the amount of ammonia present at the time of shedding can be calculated. The rate of new ammonia formation remains constant in each individual while the amount of free ammonia fluctuates considerably. By discussing the blood ammonia content in terms of these two factors it is possible to compare the results obtained by the various techniques used by the workers in this field.

The co-operation, advice and criticism of Professor J. A. Dauphinee is gratefully acknowledged.

REFERENCES

1. NENCKI, M. AND PAVLOV, J. P.: *Arch. f. exper. Path. u. Pharmakol.*, **38**: 215, 1896-7.
2. VAN CAULAERT, C. AND DEVILLER, C.: *Compt. rend. Soc. de biol.*, **111**: 50, 1932.
3. KIRK, E.: *Acta med. scandinav.*, supp., **77**: 1, 1936.
4. MONGUIO, M. AND KRAUSE, F.: *Klin. Wchnschr.*, **13**: 1142, 1934.
5. PHILLIPS, G. B. *et al.*: *New England J. Med.*, **247**: 239, 1952.
6. SHERLOCK, S. *et al.*: *Lancet*, **2**: 453, 1954.
7. MCDERMOTT, W. V., JR., ADAMS, R. D. AND RIDDELL, A. G.: *Ann. Surg.*, **140**: 539, 1954; correction, **141**: 284, 1955.
8. BESSMAN, S. P.: *Ann. Int. Med.*, **44**: 1037, 1956.
9. CONWAY, E. J. AND BYRNE, A.: *Biochem. J.*, **27**: 419, 1933.
10. CONWAY, E. J.: *Ibid.*, **29**: 2755, 1935.
11. SELIGSON, D. AND SELIGSON, H.: *J. Lab. & Clin. Med.*, **38**: 324, 1951.
12. CONWAY, E. J.: Microdiffusion analysis and volumetric error, 4th ed., Crosby Lockwood & Son, Ltd., London, 1957.
13. MCDERMOTT, W. V., JR. AND ADAMS, R. D.: *J. Clin. Invest.*, **33**: 1, 1954.
14. JACQUEZ, J. A., JELTSCH, R. AND HOOD, M.: *J. Lab. & Clin. Med.*, **53**: 942, 1959.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

A large attendance is expected at the forty-fourth annual meeting of the Canadian Medical Association, which will be held in Montreal on the 7th, 8th and 9th of June. The programme promises to be attractive. Sir James Barr, of Liverpool, one of the ablest and best known of the physicians of the north of England, is coming to deliver the address in medicine. The address in surgery will be delivered by Dr. Primrose, of Toronto. Dr. W. J. Mayo, of Rochester, will be present, and will read a paper on "Gall Stone Disease," with a view to urging early operation. No surgeons in America have had such a large experience in gall stone surgery as the Mayos. They are entitled to speak with authority, and Dr. Mayo will certainly present his views in a clear and attractive form. A number of interesting papers have been promised for different sections. Dr. Casey A. Wood, of Chicago, will read a paper before the ophthalmological section. An opportunity will be afforded the members to visit Macdonald College, which is one of the newest, largest, and most completely equipped of the agricultural colleges of the world.—Editorial comment, *Canadian Medical Association Journal*, 1: 362, April 1911.

PLASMA AND BLOOD VOLUMES IN ELDERLY PATIENTS AFTER SURGERY*

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THE FLUID shifts and blood changes that follow surgical operations have been investigated frequently. Wilkinson[1] has reported some of the more important of these and summarized the conclusions that can be drawn therefrom. This study describes the changes in plasma and blood volumes that occurred in 21 patients during the week immediately following surgery. In general, the changes observed are similar to those outlined by Wilkinson,[1] but they are reported here because they serve to emphasize the strikingly predictable pattern of the response to surgery when the postoperative course of the patient is satisfactory. Indeed, these results, together with those recorded in the literature, indicate that deviations from this pattern may be a danger signal. The results also point to the existence of an apparently constant, if usually latent, threat, because there is always present, for at least a week after surgery, a mild anemia which cannot be correlated with blood lost during operation.

Bruce[2] strongly emphasizes the value of clinical blood volume studies. Although he is far from being alone in holding this view,[3-8] such studies are carried out infrequently and reluctantly in most centres. We have examined this problem and have included some of the considerations involved and the conclusions derived therefrom.

In the experiments reported here the dextran-dilution method has been used for measuring circulating plasma volume. This method has been shown to measure accurately the circulating plasma volume and, with hematocrit determinations, the blood volume of animals and men under laboratory conditions.[9] The present series of clinical studies has provided experience with the dextran method under hospital conditions, and this report therefore includes an assessment of the method from a clinical point of view.

METHODS

The subjects were patients, almost all elderly, who had been admitted to the Kingston General Hospital for operation. Preoperative blood volumes were determined on 28 patients; of these, 22 patients actually underwent operation and 21 had uneventful recoveries. Table I shows that in none of these cases was there evidence of abnormal fluid metabolism, or that the surgery carried out could be expected to interfere specifically with fluid balance. All patients received some glucose or saline, especially during the first two days after operation, but none received blood or plasma except during the operative procedure (Table I).

Plasma volumes were measured by the dextran-dilution method; red cell and blood volumes were calculated from plasma volumes and from hematocrit estimations which had been corrected for both trapped plasma[10] and unequal cell distribution.[11] Plasma was at first analyzed for dextran by a dialysis-anthrone technique.[12] This procedure gives accurate and consistent results and presents few problems under laboratory conditions.[9] However, under clinical conditions, dialysis is not convenient. Recovery experiments have shown that the dialysis step can be replaced by an independent determination of the glucose concentration of the plasma, using a standard Sömögyi technique.[13] This technique involves some loss in the precision of the estimate but the loss is not serious and the method now presents no technical difficulties under most conditions.[14] The dextran method is safe and accurate and has several advantages; these have been discussed in detail in previous communications.[9] If a suitable dextran fraction were readily available, it could be recommended as a useful alternative to methods presently in use. Unfortunately a suitable preparation is not on the market, so that at this time such a recommendation can be of academic interest only.

RESULTS

Control measurements, which were made within a day or two after admission to hospital, did not indicate that advancing age results in any predictable change in blood volume. Several workers have suggested that relative blood volume may decrease with age;[15, 16] the results of this study lend no support to this idea. Thus the average blood volume for 19 females (17 of whom were over 55 years of age) was 4.2% greater than the volume that would be predicted for this group on the basis of their sex and physical characteristics but regardless of age. Predictions were based on the formulae proposed by Allen and his colleagues.[17] The 12 males observed had an average control blood volume that was 2.3% greater than the average predicted volume. These differences from predicted volumes were not significant.

Results of plasma and blood volume determinations carried out in each patient during the six days that immediately followed surgical operation are listed in Table II. In general there was a decrease in plasma volume during the first day or two after operation and increases thereafter. Fig. 1 illustrates the average changes in plasma, red cell and blood volumes that took place during the six days that followed surgical operation.

Hematocrit percentages (Table III) decreased steadily throughout the first five postoperative days and averaged about 2% below controls on day one, 11% on day three, and about 12.5% below controls

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TABLE I

Patient					Parenteral fluid						
					During operation		During days after operation (glucose and/or saline)				
No.	Age	Sex	Diagnosis	Surgical procedure	Blood	Glucose and/or saline	1	2	3	4	5
	Yrs.				L.	L.	L.	L.	L.	L.	L.
1	72	F	Hemorrhoids, rectal adenoma	Hemorrhoidectomy, fulguration of rectal adenoma	—	0.5	0.5	—	—	—	—
2	72	M	Perforated pyloric ulcer, sec. adeno-ca. of liver	Closure of ulcer, gastrojejunostomy	0.8	4.5	2.0	2.5	2.5	—	—
4	69	F	Ca. right breast, metastases	Simple mastectomy, removal of pectoralis major. Rotation flap after normal dehiscence	—	0.5	1.5	—	—	—	—
5	58	F	Reticulum cell sarcoma, right axilla	Excision of mass in axilla	—	1.0	—	—	—	—	—
8	68	F	Duodenal ulcer, calculus cholecystitis, diaphragmatic hernia	Subtotal gastrectomy, cholecystectomy	0.4	—	2.0	3.0	3.0	3.0	2.0
10	72	F	Prolapse uterus, ca. pancreas	Le Fort operation	—	—	—	1.5	1.0	—	—
11	73	F	Prolapse uterus, rectocele, cystocele	Ant. and post. colporrhaphy and perineorrhaphy. Modified Le Fort	—	0.3	1.0	—	—	—	—
12	50	M	Ca. rectum (incl. sacrum and prostate)	Abdominoperineal resection, prostatectomy, cystostomy	2.0	1.4	1.5	3.0	2.0	2.0	—
17	58	F	Ca. left breast (Stage II)	Left radical mastectomy	0.8	1.0	2.0	—	—	—	—
18	67	M	Calculus cholecystitis	Cholecystectomy	—	1.8	2.0	—	—	—	—
20	70	M	Ca. right lung	Lobectomy, right lower lobe (wound dehiscence)	0.8	3.0	3.0	—	—	—	—
21	73	M	Ca. scrotum	Part. scrotectomy, right orchidectomy, block dissection of right subinguinal lymph nodes	—	1.0	—	—	—	—	—
22	63	F	Ca. rectum	Abdominoperineal resection	0.4	1.5	3.0	3.0	2.0	2.0	—
23	64	M	Gastric ulcer	Partial gastrectomy, anastomosis	0.4	1.0	2.0	3.0	3.0	2.0	—
24	75	F	Ca. left breast, met. axillae	Left simple mastectomy	0.4	2.5	—	—	—	—	—
25	84	M	Ca. rectum, met. to liver	Laparotomy, coag. rectal ca.	0.4	0.5	2.4	—	—	—	—
26	67	M	Ca. hepatic flexure colon	Right hemicolectomy	0.4	1.5	3.0	2.5	3.0	3.5	5.0
27	58	F	Cholecystitis and cholelithiasis	Cholecystectomy, choledochectomy and appendectomy	—	1.5	2.5	2.0	2.0	1.0	—
28	63	F	Ca. rectum	Abdominoperineal resection	1.2	1.5	3.0	3.0	3.5	2.5	0.8
30	60	F	Cholelithiasis and empyema of gallbladder	Cholecystectomy	—	2.5	2.0	—	—	—	—
31	75	F	Thyroid ca.	Left (thyroid) lobectomy	—	1.0	—	—	—	—	—

on day five. These hematocrit measurements combined with the plasma volume measurements gave average red cell and blood volume changes that are illustrated in Fig. 1. Cell volumes measured one to two days after operation were, on the average, about 12% below control volumes. During the next two days, there was a more gradual decrease (to about 18% below controls). Blood volumes decreased during the first two postoperative days and increased thereafter so that, five or six days after surgery, the total circulating blood volumes were not significantly different from those of controls (Fig. 1).

DISCUSSION

As is the case with most clinical investigations, there are in this study a large number of uncontrolled variables. Thus the subjects differ from one another with respect to pathology of their disease, extent and nature of surgical procedure, postoperative food intake and in a number of other ways. In spite of these conditions, however, the postoperative changes in blood and plasma volumes are remarkably consistent. For example, there was a modest decrease in plasma volume in all but two subjects 24 to 48 hours after operation (Table II). It is possible that such a decrease occurred in these two and that it was not apparent only because the first postoperative measurements were made on the second rather than on the first day after the operation. Further, Tables II and III show that these decreases in plasma volume are usually accompanied by decreases in hematocrit readings; when increased hematocrit readings are observed the increases are small as compared with the concomitant decreases in plasma volume. Thus during this early postoperative period the decreases in plasma volume are accompanied, in all but three instances, by decreases in cell volume.

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TABLE II.—PLASMA VOLUMES AS % OF CONTROLS

No.	Control	Days after operation					
	L.	1	2	3	4	5	6
1	2.61	—	—	—	121.8	—	—
2	2.35	—	111.5	—	125.9	—	—
4	3.31	—	—	—	94.5	—	—
5	3.40	—	—	—	—	110.2	—
8	1.84	—	85.9	—	—	125.5	123.3
10	2.72	—	87.9	—	82.3	—	94.9
11	2.26	—	—	90.3	—	—	—
12	2.52	86.1	—	—	119.8	—	135.3
17	2.73	97.8	—	—	111.7	—	108.4
18	2.42	88.8	—	—	—	107.9	—
20	3.30	86.4	—	107.9	—	—	117.3
21	3.50	94.3	—	96.6	—	103.1	—
22	2.09	—	103.8	—	100.9	—	94.7
23	2.64	—	89.8	—	93.6	—	94.3
24	2.49	94.4	—	81.9	—	—	93.6
25	4.01	—	81.8	—	78.3	—	84.8
26	2.85	97.5	—	89.1	—	—	110.5
27	2.35	89.4	—	114.0	—	122.9	—
28	2.00	—	93.5	—	137.5	—	119.5
30	2.66	98.9	—	107.9	—	112.4	—
31	3.01	86.4	—	—	—	97.7	—

Changes in plasma volume that were observed from the second to the sixth postoperative day are also consistent. During this period 16 of 17 subjects showed increases in plasma volume; 13 of these can be reported as major increases (Table II).

A detailed comparison of these results with results obtained by others is difficult, firstly because there seem to be few studies which are strictly comparable, and secondly because in some of the studies that are quite similar the results are presented in insufficient detail. Where results can be compared there is a real measure of basic agreement, particularly in respect of plasma volume changes. Thus Likoff and his colleagues[7] made serial measurements on 10 patients and noted decreases in plasma volume the first day after operation; the decreases reported by this group were of the same order of magnitude as those reported here. Similar plasma volume changes have been reported by Smolik *et al.*[18] and by Finley and his colleagues.[19] The decreases in red cell volume that we observed the first day or two after operation are similar to those observed by the Likoff and Smolik groups.[7, 18] Finley *et al.*,[19] however, reported increases in hematocrit together with decreased plasma volume, increases which in some cases indicated an actual increase in the volume of red cells in the circulation. This group, however, observed changes that resulted from drastic thoracic surgery and involved large infusions of blood.

TABLE III.—POSTOPERATIVE HEMATOCRIT VALUES EXPRESSED AS PERCENTAGES OF CONTROLS

Patient No.	Control Hematocrit	Days after operation					
		1	2	3	4	5	6
	%						
1	41.4	—	—	—	88.0	—	—
2	45.7	—	82.2	—	82.0	—	—
4	41.2	—	—	—	84.7	—	—
5	35.0	—	—	—	—	96.0	—
8	35.8	—	93.0	—	—	79.3	81.9
10	32.6	—	105.9	—	98.8	—	96.9
11	38.8	—	—	84.3	—	—	—
12	33.4	102.0	—	—	86.8	—	79.6
17	43.7	97.2	—	—	90.2	—	85.1
18	47.5	105.0	—	102.4	—	94.7	—
20	44.6	83.1	—	80.2	—	—	80.8
21	40.2	94.4	—	96.0	—	89.3	—
22	38.8	—	91.0	—	85.3	—	87.2
23	36.6	—	108.1	—	104.3	—	97.0
24	39.4	94.9	—	87.3	—	—	82.5
25	36.9	—	113.2	—	111.9	—	97.8
26	35.8	105.7	—	97.3	—	—	92.5
27	29.8	103.0	—	81.9	—	82.9	—
28	38.0	—	79.4	—	67.4	—	65.0
30	38.4	91.6	—	81.3	—	82.3	—
31	39.9	99.4	—	96.3	—	88.9	—

The postoperative decrease in plasma volume is usually attributed to a movement of fluid from the circulating plasma into the injured tissues.[1] There is no good reason for questioning the occurrence of such a shift, yet if it is not accompanied by a concomitant escape of red cells the result must be hemoconcentration. We, as well as the others cited above, observed no hemoconcentration one to two days after operation, times at which plasma volume is still reduced. On the contrary, there was a reduction in cell volume, a reduction almost always equal to and usually greater than the accompanying reduction in plasma volume, and the cell volume continued to decrease for from three to five days after operation.

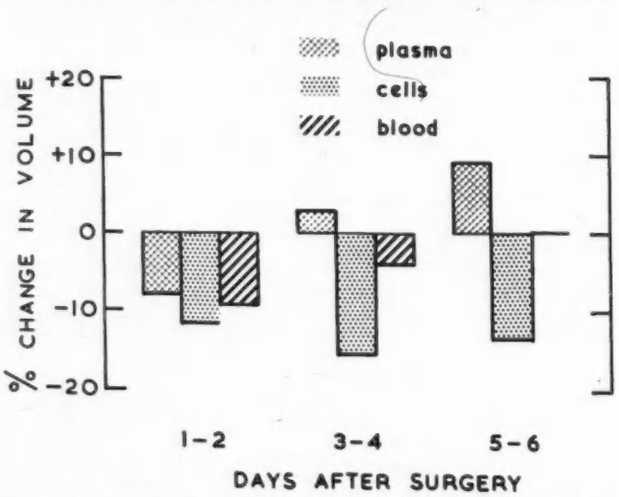

Fig. 1.—Mean postoperative changes in plasma, red cell and blood volumes in 17 patients.

A number of investigators have discussed the mechanisms that might be responsible for this apparent cell loss in the absence of any overt wound bleeding or seepage.[18, 20] In our opinion the most likely explanation is that, after operation, relatively large numbers of cells undergo destruction. It may be that injury, surgical or other, actually brings about a change in the rate of normal cell removal, but it would seem more reasonable to postulate that there are circulating, after surgery, a larger proportion of cells which are ripe for removal by normal processes. The mechanical trauma involved and the resulting chemical changes may alter many cells so that, in effect, they become prematurely senescent. Then, too, during most operations some blood is administered to replace the surgical loss. Our series is typical in that 11 of the 17 subjects on whom serial measurements were obtained re-

ceived at least one bottle (400 ml.) of blood that had been stored in acid-citrate-dextrose. There is no doubt that many cells, thus stored, have subsequently a shorter life, *in vivo*, than is normal. An analysis of our results (Table IV) indicates that, on the average, there is a greater loss of cells from the subjects who received during their operation large amounts of blood than there is from those who received either one bottle or none at all. If even a portion of the decrease in cell volume that is observed in subjects who received no transfusion can be attributed to blood lost during operation, Table IV indicates a correlation between volume of transfusion and post-surgical blood cell loss. On the other hand, large transfusions are in general associated with more injury, so that the relationship shown by Table IV may also involve the removal of endogenous erythrocytes.

TABLE IV.

Volume of blood transfused	*No. of subjects*	*Cell volume as % of control volume*
ml.		
0	6	91.1
400	6	93.7
800+	5	78.2

Reduction in cell volume one to two days after operation shown with subjects grouped according to the amount of blood received by transfusion during operation.

There may be no real reduction in cell volume at all. The possibility exists that the reduction is apparent only and comes about as a result of a postoperative redistribution of red cells. Chaplin, Mollison and Vetter[11] have shown that in normal humans the body/venous hematocrit ratio is 0.91 over a wide hematocrit range; together with others,[7, 18, 19] in noting post-surgical decreases in cell volume, we have assumed that no change occurs in this ratio as a result of surgery. In a calculation of cell volume from plasma volume and hematocrit a change in the body/venous hematocrit ratio to 0.97 or 0.98 would account for the average decrease in cell volume noted in our subjects 24 to 48 hours after operation (Fig. 1). Such a change in the ratio would, in fact, involve a local concentration at some as yet unrecognized site, a possibility suggested by a number of workers.[18, 20] A series of experiments such as those reported here, but in which cell volumes are measured independently of plasma volumes, would seem in order. Because relatively small differences would be involved, such a study would demand both individually accurate measurements and a respectably large number of subjects.

If the apparent loss of cells is the most interesting aspect of this study from a physiological standpoint, the consistent hemodilution (and thus the mild anemia) is the outstanding clinical consideration. Because total blood volumes are often normal or even above normal, infusions of whole blood are not always indicated. Infusions of packed cells together with measures that assist the hemopoietic mechanisms should be considered if the anemia is considered a threat.

A study of the hematocrit values listed in Table III, together with the overall volume picture that results when the hematocrits and plasma volumes are considered together, underlines the point stressed by Bruce[2] and many others[7, 19-23] that hematocrit percentages alone are of little or no value in assessing circulatory condition. Surgical operations bring about no change in cell size or in the hemoglobin content of red cells,[20] so that hemoglobin determinations offer no additional information. The literature indicates that these facts are well known, yet in many hospitals blood volume determinations are actually viewed with alarm. A reasonable familiarity on the part of every clinician with the various blood volume methods available, together with an idea of their application and limitations, would overcome this attitude. An enormous amount of data attests the accuracy and reliability of several methods, including the use of T-1824 and I^{131}-labelled albumin methods, the dextran method and the Cr^{51}-labelled cell technique. Each method has its own specific advantages and limitations under a given set of clinical conditions, but for general hospital use any one might be adopted and be generally useful. Modest technical problems are associated with each method, and in this respect the method of choice is a matter of personal experience and opinion. Certainly there is no economic basis for avoiding volume determinations; the equipment required is well within the reach of small hospitals.[6] Methods for measuring blood volume, it is true, do not lend themselves to "mass production" and for this reason overworked hospital laboratories are often quite unenthusiastic about adopting them. It is also true that the determinations require a conscientious worker who is interested in the investigation and who can intelligently interpret the results obtained. There is no electronic substitute for such a person. The truth is simply that the information obtained from a satisfactory blood volume determination can be obtained in no other way. This information is almost always useful, and is often invaluable, in assessing the circulatory condition of the patient.[2, 8, 24] Failure to make the modest effort required to establish and operate the facilities for reliable volume determinations is inexcusable.

SUMMARY

Plasma volumes were measured by the dextran-dilution method and blood volumes were calculated from the plasma volume and hematocrit values of 28 elderly patients on admission to hospital. Serial post-operative volumes were determined in 21 of these patients, all of whom were in satisfactory clinical condition.

Preoperative volume measurements indicated that there is no predictable change in plasma or blood volume with advancing age.

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Postoperative measurements showed that during the first day or two after operation there is a decrease in both plasma and cell volumes. The decrease in cell volume is usually slightly greater than the concomitant decrease in plasma volume, so that at this stage there is usually mild hemodilution with a decreased total blood volume. Plasma volume increases from about the second to about the sixth postoperative day, while cell volume continues to decrease for four to five days after operation. At this stage a moderate hemodilution is observed, combined with a normal or somewhat increased total blood volume.

Possible mechanisms which account for the loss of cells are discussed.

The value of clinical blood volume determinations is emphasized.

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REFERENCES

1. WILKINSON, A. W.: Body fluids in surgery, E. & S. Livingstone, Ltd., Edinburgh, 1955.
2. BRUCE, J.: *Canad. Serv. M. J.*, **13**: 728, 1957.
3. BELING, C. A., MORTON, T. V. AND BOSCH, D. T.: *Surg. Gynec. & Obst.*, **87**: 163, 1948.
4. WILSON, W. C.: *Edinburgh M. J.*, **57**: 30, 1950.
5. BERLIN, N. I. *et al.*: *New England J. Med.*, **247**: 675, 1952.
6. PARSONS, W. H., WILLIAMS, W. T. AND FORSYTHE, L. J.: *Ann. Surg.*, **135**: 791, 1952.
7. LIKOFF, W. *et al.*: *Am. Heart J.*, **50**: 163, 1955; correction, **50**: 954, 1955.
8. PEDEN, J. C. *et al.*: *Ann. Surg.*, **151**: 303, 1960.
9. SEMPLE, R. E., THOMSEN, A. E. AND BALL, A. J.: *Clin. Sc.*, **17**: 511, 1958.
10. ROOT, W. S., ROUGHTON, F. J. W. AND GREGERSEN, M. I.: *Am. J. Physiol.*, **146**: 739, 1946.
11. CHAPLIN, H., JR., MOLLISON, P. L. AND VETTER, H.: *J. Clin. Invest.*, **32**: 1309, 1953.
12. SEMPLE, R. E.: *Canad. J. Biochem. & Physiol.*, **35**: 383, 1957.
13. SÖMÖGYI, M.: *J. Biol. Chem.*, **90**: 725, 1931.
14. SEMPLE, R. E.: Prepared for publication.
15. SKLAROFF, D. M.: *Am. J. Roentgenol.*, **75**: 1082, 1956.
16. WENNESLAND, R. *et al.*: *J. Clin. Invest.*, **38**: 1065, 1959.
17. ALLEN, T. H. *et al.*: *Metabolism*, **5**: 328, 1956.
18. SMOLIK, E. A. *et al.*: *Surg. Gynec. & Obst.*, **104**: 565, 1957.
19. FINNEY, R. K., JR. *et al.*: *J. Thoracic Surg.*, **22**: 219, 1951.
20. STANTON, J. R. *et al.*: *Surg. Gynec. & Obst.*, **89**: 181, 1949.
21. ALLBRITTEN, F. F. *et al.*: *J. Thoracic Surg.*, **19**: 71, 1950.
22. BELING, C. A., BOSCH, D. T. AND MORTON, T. V.: *Surg. Gynec. & Obst.*, **90**: 686, 1950.
23. WASMUTH, C. E. *et al.*: *Cleveland Clin. Quart.*, **22**: 124, 1955.
24. CREHAN, J. P.: *S. Clin. North America*, **34**: 605, 1954.

LEPROSY IN CANADA*

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LEPROSY DOES not now exist in indigenous form in Canada, owing to careful public health control measures. However, vast reservoirs of infected population still exist, especially in India, China and the tropics. The disease is very often slow in progress and frequently an affected person may not exhibit the leonine face or eroded extremities so firmly fixed in the public mind as the typical picture. With the great increase in international travel far more cases are arriving in lands where physicians are not familiar with what is a relatively common disease in the Far East. In 1959, there were 21 known cases in Canada, and two were diagnosed in 1960 in Alberta.

The present report concerns one of these cases, a Hindu who remained undiagnosed in a traveller's odyssey which began in 1956 in Calcutta, passing through Persia, Arabia, Athens, Bulgaria, the Soviet Union, Mongolia, China, Czechoslovakia, Poland, Finland, Germany, Austria, Italy, France, Holland, Denmark, Sweden, Great Britain, Ireland, the United States including Alaska, and Canada by 1960. During this period he had six hospital admissions in Odessa, Britain, the U.S.A., and Canada without diagnosis of his disease. The purpose of this paper is to review some of the major features of this disease and appropriate diagnostic techniques to alert physicians who deal with immigrants from areas where leprosy is endemic.

Medical knowledge of leprosy has shown that it is of much lower infectivity than tuberculosis, is often a very indolent disease indeed, and is responsive to sulfones and methimazole (Tapazole) therapy.

CASE REPORT

The patient, a Hindu electrical engineering student, states that he set off on an attempted world tour by motor cycle from Calcutta in 1956, bearing a placard "U.S.S.R., Europe, U.K.". Apart from a fever thought to be due to malaria in India, he had previously been healthy and he gave no family history of disease. After a falling masonry block bruised his right hand in 1956, he noticed the slow development of a clawing deformity. This consisted of flexion in the distal phalanges and slow anterior subluxation of the proximal interphalangeal joints of the second and third fingers. This was quite painless and he drove in 1957 through Persia, Arabia, Athens, the Soviet Union, Mongolia and China. While in Odessa he was hospitalized for severe abdominal pain and was discharged without a definite diagnosis. Reaching Prague he was treated for "swelling of the left foot". After travelling through Europe he was again hospitalized for another bout of severe abdominal pain with diarrhea and melena in England. This cleared spontaneously after several days. He states that he partly worked his way by making appearances on television networks in Bulgaria, Moscow, and Great Britain en route.

Later, in Toronto, in January 1958, he developed high fever and generalized aching. On admission to hospital, wasting of the small muscles of his hands

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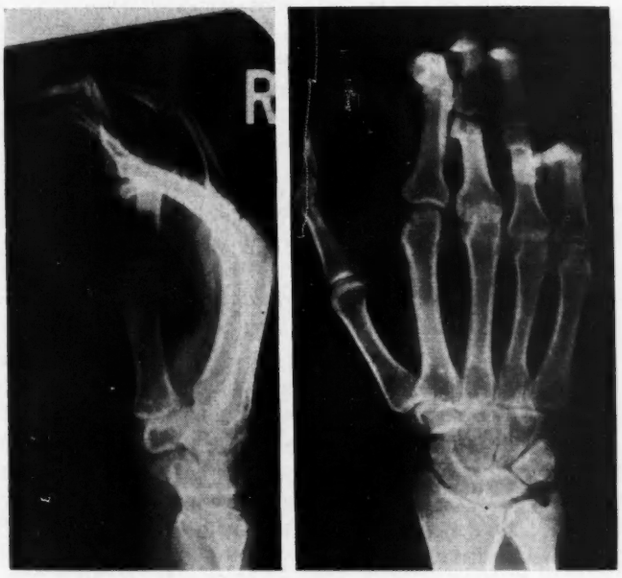
Fig. 1.—A diffuse bronze macular rash covers the wrists. Wasting of the small muscles of the hands, flexion contractures of the fingers and volar subluxation of some interphalangeal joints are present.



a b

Fig. 2.—Neuropathic claw hand shown by progressive distal osteoporosis, narrowing of distal phalanges with loss of tufts, interphalangeal subluxations and very marked soft tissue atrophy.

was noted and large soft painless lymph nodes were felt in the left groin and axilla. Investigation showed positive tests for occult blood in the stool on two occasions. This illness was diagnosed as Asian influenza. He apparently recovered on salicylates only. Reaching Vermont, U.S.A., he noticed small sores appearing on the soles of his feet and recognized that he could be frost-bitten very easily without realizing it. Later he crashed on his motor cycle, lacerating the palm of his left hand which was treated by skin grafting in hospital in San Diego, California. Three weeks later he noted the development of similar contractures in this hand.

In 1959, at Oliver, B.C., stricken by another attack of fever and abdominal pain he was treated conservatively for possible appendicitis. Loss of temperature discrimination was becoming more evident, for he had a hot water bottle burn to the sole of his left foot, to his surprise, during his stay in hospital. He was admitted to the Calgary General Hospital in February 1960 with a history of a weight loss of 20 lb. over the past two years, generalized weakness and muscle wasting of his hands, unexplained bouts of fever and "neuralgic" pains, especially in his limbs. He was discharged after 18 days without a definite diagnosis. About this time he noted a blotchy purplish papular rash, appearing over the wrists and ankles, which seemed to become nodular and to wax and wane. Occasionally the papules would be extremely painful and sensitive as they appeared. Re-admitted in July 1960, he was found to have bouts of intermittent evening temperature up to 102° F. lasting about three weeks, followed by a similar period of apyrexia, as on the previous admission.

Physical examination revealed a slender, intelligent, Indian, without facial abnormality or nasal discharge, and with shotty pea-sized tender lymph nodes in both posterior cervical triangles. The trunk showed no changes. The hands showed a mixture of neuropathic abnormalities with considerable weakness of grip and some deformity (Fig. 1). The radial nerves were chiefly affected, with almost complete loss of extensor power and moderate flexion clawing deformity of the terminal finger phalanges. The ulnar nerve was least affected, with some wasting of the interossei and hypothenar muscles, but unopposed activity of the lumbricals had occurred with flexion of the metacarpophalangeal joints and overextension of the proximal interphalangeal joints producing the anterior subluxation deformity seen in Fig. 1. Marked median nerve pareses were also present with flattening of the thenar muscles and paralysis of the flexor digitorum sublimis, giving rise to the subluxation described. A flat "monkey's paw" hand with some clawing had resulted. Both ulnar nerves were thickened and palpable but were not tender. The wrists and hands showed moderate diffuse bronze pigmentation and unusual induration of the otherwise parchment-like skin on which there was complete absence of sweating or hair. A "glove" type of anesthesia to pin-prick coincided with the bronze

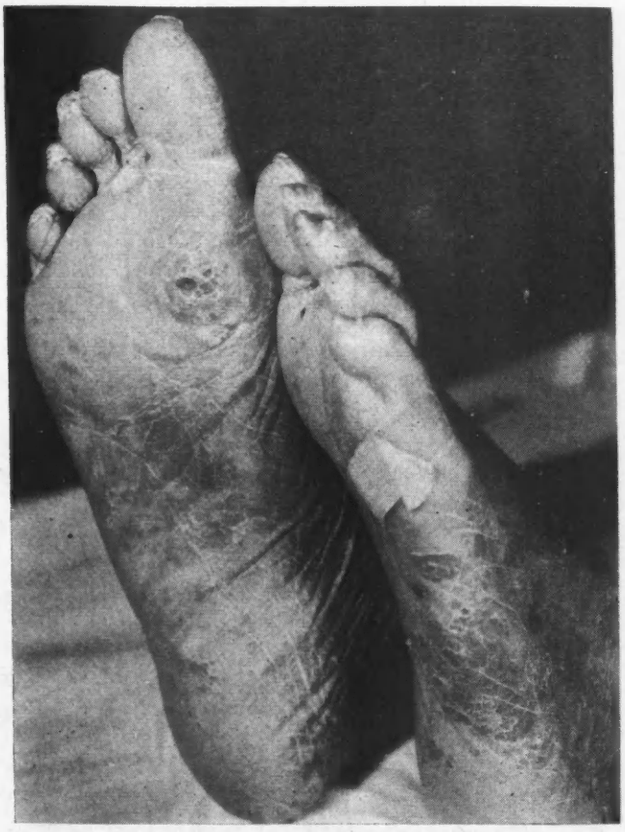


Fig. 3.—A papular rash extends from the ankles over the soles, with an insensitive trophic ulcer on the ball of the great toe.

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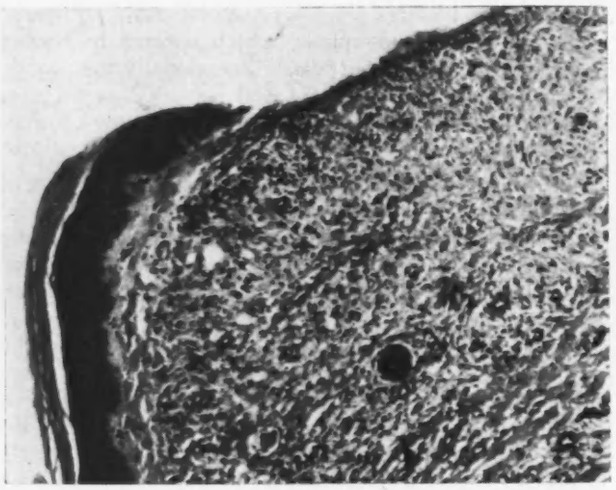


Fig. 4.—Biopsy of lepromatous nodule of knee. Dense packing of the dermis by lepra foam cells is present, with a vague tuberculoid pattern at the upper right.

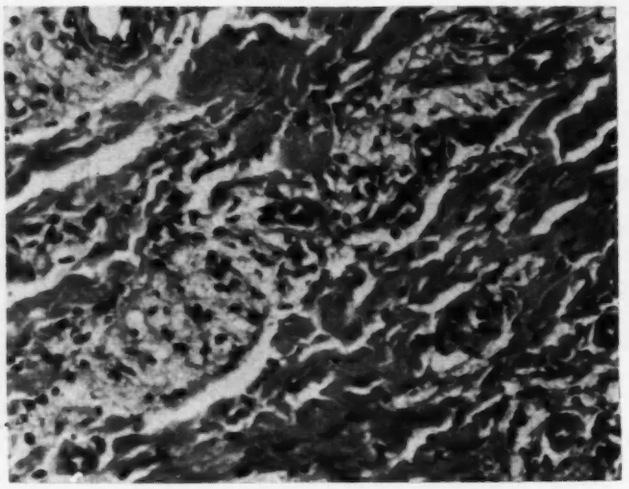


Fig. 6.—Lepra foam cells surround a cutaneous nerve bundle.

pigmentation. Temperature discrimination was absent in the hands and impaired on the forearms. Radiographs of the hands were reported as indicative of rheumatoid arthritis, but did not show the spindle-shaped joint swellings and decalcification typical of this disease (Fig. 2).

A raised, circumscribed, soft, circular reddish plaque of skin thickening, 2 cm. in diameter, was present over the left patella, simulating keloid formation. This was biopsied. Both ankles had an edematous appearance, with bronze pigmentation and changes as on the wrists. In addition the reddish-blue confluent nodular thickening of the skin extended over the ankles to the hypothenar margins of the soles (Fig. 3). A "sock" pattern of absent temperature discrimination and anesthesia to pin-prick was present over both feet and the lower third of both legs. Sensitivity to light touch and vibration sense were unimpaired as in the arms. Except for a small area at the base of the plantar surface of the left great toe, the soles of the feet were anesthetic to pain. Over the ball of the right great toe there was a completely anesthetic punched-out trophic ulcer, 3 mm. in diameter, and a similar lesion over the ball of the left little toe. On these clinical grounds leprosy was diagnosed by one of us (B.F.), who had previously seen a case.

Laboratory Investigations

The hemoglobin value was 12.8 g. %, sedimentation rate 46 mm./hr. (Wintrobe), and the leukocyte count was 14,100/c.mm., 83% of which were neutrophils.

Serum electrophoresis showed a total protein value of 8.7 g. %, with albumin 19%, and alpha-2 globulin 15%.

The V.D.R.L. reaction was negative, which was somewhat unexpected in view of the abnormal electrophoresis, since these patients often show a false positive Wassermann reaction.

The bromsulfalein excretion test was mildly abnormal with 12% dye retention after 45 minutes. Cephalin flocculation was three plus; the Congo Red test for amyloidosis showed no abnormalities. The blood urea nitrogen level was normal.

Biopsy of the skin nodule on the left knee showed a dermis filled by small foam cells with eccentric nuclei giving the appearance of a lepromatous nodule (Figs. 4, 5 and 6). A modified Ziehl-Neelsen stain revealed that these cells were packed with vast numbers of short, pallisaded, beaded, acid-fast bacilli which were

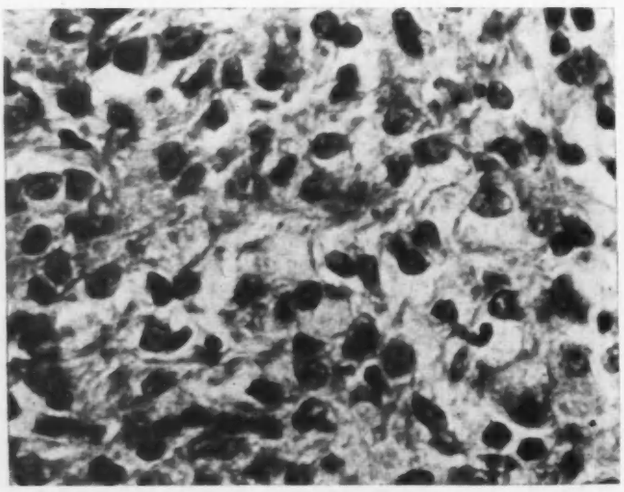


Fig. 5.—High-power view of lepra foam cells in the dermis of the leproma. Hematoxylin, phloxine and saffron.

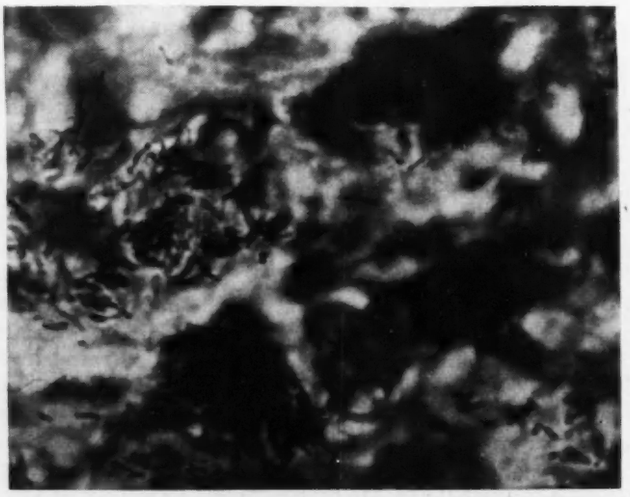


Fig. 7.—Modified Ziehl-Neelsen stain shows bundles of bacilli living in lepra cells.

not spirit-fast and therefore resembled *Mycobacterium leprae* (Fig. 7). Sternal bone marrow films had showed a mild increase in granulocytic activity, but, on restaining, a few solitary bacilli resembling *M. leprae* were found inside mononuclear cells which were not of foamy type. Nasal smears were consistently negative for bacilli, but severe epistaxis followed each nasal swabbing. The urine on several occasions showed no abnormalities, but sediment from 24-hour samples on staining yielded a few morphological *M. leprae*. These changes all pointed to typically silent, but widely disseminated, disease.

The patient was given diamino-diphenyl sulfone, 1 g. daily, and over the next six weeks his trophic ulcers healed. The skin nodules are little altered and the neuropathic contractures and pains have slowly progressed. Occasional melena has also occurred.

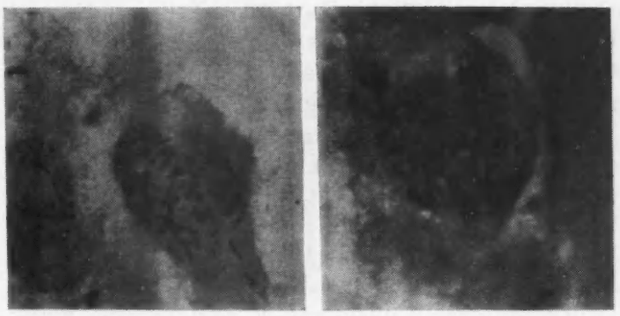
Bacteriological Studies

Vast numbers of *M. leprae* may exist in the intact lepra cells without necrosis, but are undetectable by conventional Ziehl-Neelsen stain. With the minor modification of eliminating alcohol decolourization they are easily seen (Fig. 7). Research on treatment has been seriously hampered by the complete failure of all attempts over the years to grow these bacilli on artificial media. They appear to be obligatory intracellular parasites. A biopsy of the lepromatous nodule, placed in saline, was therefore flown to the Virology Laboratories of the Medical School of the University of Manitoba, with a request that tissue culture of this specimen be attempted. The following report was received:

"The material was ground and placed on monkey kidney tissue culture which contained two cover slips; it was also placed on two tubes of amnion. No cytopathogenic effect was observed. Acid-fast stains on the cover slips showed intracytoplasmic acid-fast bacilli singly and in clumps resembling leprosy in a tissue biopsy. The amnion cells were scraped from the surface of the tube, smears were made on slides, and acid-fast stains made. Similar organisms were seen within the cells as with the monkey kidney cover slips (Fig. 8). The supernatant fluid from the tissue culture and ground-up tissue culture cells were repassed to monkey kidney and were negative. This passage from the primary culture is being repeated. Tissue culture fluid and infected tissue culture cells were also inoculated into guinea pigs and cultured on Petragnani, blood agar, broth, and thioglycolate; all remained negative. In summary, we apparently obtained a first passage on tissue culture but failed in a second passage."

DISCUSSION

The outlook for patients with leprosy has been transformed during the past 15 years. In general, leprosy can be arrested by the bacteriostatic effect of sulfones.[1] Those patients in advanced stages fortunately react most promptly, and the first sign of improvement is usually regression of mucosal lesions. These begin to disappear after 6 to 12 months of treatment. However, treatment for two to five years is generally necessary for the patient to become completely bacteriologically negative.[2] While bacteria disappear from the skin first, they do persist longest in cutaneous nerves. Clinically, neuritic pain is the last symptom to disappear. As a result a great deal can be accomplished by remedial surgery designed to correct deformities produced by the pull of muscle groups which are unevenly balanced by nerve lesions.



a b

Fig. 8.—Shows two monkey kidney tissue culture cells. Acid-fast bacilli are present within the cytoplasm of the cells singly and in clumps. Organisms within these cells are similar to the organisms in the cells of the biopsy.

In addition the tuberculostatic drugs all appear to have a beneficial effect similar to that of the sulfones. Their use is limited only by the long term of maintenance therapy needed, and at present they are used at the start of treatment to heal skin lesions promptly. The most recent advance has been the rapid clinical response of leprous patients to methimazole (Tapazole[3]) and thiourea derivatives.

It is not always appreciated that leprosy has an exceedingly long natural history. This has led to its inordinately bad reputation in the public mind, for these patients survived so many decades with crippling neuropathic deformities or visible mutilation of the face. In the resurgence of the disease in the Middle Ages, when no treatment was yet known, sufferers were expelled from society by invoking remote Old Testament dictates, for there were no public health laws at that time. In Leviticus, chapter 13, it states, "and the leper in whom the plague is, his clothes shall be rent and his head bare and he shall put a covering upon his upper lip, and shall cry, unclean, unclean. All the days wherein the plague shall be in him he shall be defiled; he is unclean; he shall dwell alone; without the camp shall his habitation be." This "covering of the upper lip" must be one of the earliest recorded uses of the surgical mask.

After the bubonic plagues of the "Black Death" few leprosy patients survived, for they are most susceptible to secondary infections and many of their deformities are in fact due to these. The disease has largely vanished in Europe since this time, apart from occasional small foci, for example in Norway and Iceland.

It is stated that "in New Brunswick the history of leprosy can be traced back to 1758, when it is said that French sailors from the *Indienne*, a vessel trading with the Levant, which was shipwrecked at the mouth of the Miramichi, spread the disease to the fisherfolk who gave them shelter."[4] It is also possible that the disease was reintroduced there by early French settlers from the region of St. Malo in Normandy, which was then a leprous district.[5]

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With isolation at Tracadie, N.B., the disease became extinct. Since this time the instances seen in Canada have been essentially of imported type[6] and no endemic foci have endured.

That this is not due to any lack of contact is shown by the number of cases in Canada known yearly to the Department of National Health and Welfare. This rose from four instances in 1921 to 12 by 1951, and 21 by 1959. As in the case reported here, the diagnosis has often been unrecognized for considerable periods in many instances, one remaining undiagnosed in Ontario for 16 years.[7] This in itself is good evidence of the very low infectivity of the disease.

While medically this is known to be true, in the public mind leprosy is associated with the false belief of extreme infectiousness.

It is of interest to note the racial origin of the total known cases in Canada in 1959: Chinese 12, Japanese one, Russian three, Lithuanian one, Canadian four (two French Canadian, one British Canadian, one Irish Canadian). Of these, 16 are now continuing treatment at home as outpatients under medical supervision. The Quarantine, Immigration Medical and Sick Mariners Services, Department of National Health and Welfare, are responsible for insuring the care and treatment of all these patients. They maintain a hospital at Tracadie, New Brunswick, as a leprosarium. It is through such interest that the disease has never gained a foothold in Canada despite contacts. Sometimes in these immigrant cases the patients have lived in close contact with many residents, but in the last 50 years no secondary case has ever developed in Canada with the solitary exception of an immigrant family group.[8]

SUMMARY

With the great increase in international travel, leprosy is being seen in countries where it is not endemic. The features of one case are described. This patient was a Hindu, who made a traveller's odyssey from Calcutta to Greece, the U.S.S.R., China, Mongolia, almost every country in Europe, the U.S.A., and Canada, with numerous television appearances and six hospital admissions en route without the condition being diagnosed.

The prognosis for these patients has been transformed in the past 15 years with the introduction of sulfones, methimazole, and thiourea derivatives. Patients with advanced disease respond most promptly and can be made bacteriologically negative in two to five years.

The history of the disease in Canada provides good evidence of its extremely low infectivity, which is much less than that of tuberculosis. A partly successful attempt to propagate the *Mycobacterium leprae* serially on tissue culture, using amniotic and monkey kidney cells, is also recorded. This may have important implications for the investigation of therapeutic agents in this disease.

We wish to acknowledge the availability of comprehensive information on leprosy for Canada which was readily provided by Dr. W. H. Frost, Chief of the Quarantine, Immigration Medical and Sick Mariners Services, Department of National Health and Welfare, and for Alberta by Dr. A. Somerville, Deputy Minister of Health, Province of Alberta.

REFERENCES

1. DOULL, J. A.: *J. A. M. A.*, **173**: 363, 1960.
2. MANNWEILER, E.: *German M. Month.*, **5**: 24, 1960.
3. KURZ, P. L.: Medical Director, Eli Lilly Clinical Research International, Indianapolis: Personal communication.
4. Hospital Service Department Notes: *Canad. M. A. J.*, **26**: 735, 1932.
5. RUTTAN, H. R. AND WRONG, N. M.: *Ibid.*, **78**: 19, 1958.
6. KANEE, B.: *Ibid.*, **73**: 284, 1955.
7. USHER, B.: *Ibid.*, **24**: 693, 1931.
8. BROWN, C. P.: Cited in *Ibid.*, **78**: 19, 1958.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE SITUATION IN ONTARIO

The medical situation in Ontario is interesting at the moment, and it is evident that the time for a careful revision of the whole question of standards and authority must receive the attention of the government. The "University Medical Bill' has called for no end of comment, and has aroused the many opponents of the university to action, so that it seems probable that no legislation will be enacted this session. The most vulnerable clause in the Bill is that asking for increased university representation in the council. Undoubtedly this request is unwise in view of the state of public feeling, and the situation is rendered more interesting by the fact that the osteopaths are pressing warmly for recognition, and are encouraged by undoubted sympathy in quarters not far removed from government circles. The members of the medical council received a sharp rebuff from Premier Whitney, who has at least the courage of his convictions, whether right or wrong, when they attempted to force the situation by calling on him without an appointment, and it is felt that they may at least wake up to the fact that they must reform. In the University of Toronto the cry is "fight for the absolute right to register our graduates"; outside of that circle there is evidently a desire to compromise, and several excellent suggestions are made. One is that university examinations in primary subjects be accepted by the council and its power to conduct final examinations be retained. Another is that council examinations be done away with altogether and assessors appointed. Be that as it may, the general feeling is that something must be done, first to relieve the students of the enormous fee gathered by the council; second to get rid of the dual examination. If Queen's University and Toronto would stand shoulder to shoulder, they could force the whole situation and put medical education on a high plane. Unfortunately, Queen's is unnecessarily suspicious of anything emanating from Toronto, whether in arts, medicine, or science. Constant rivalry makes the Queen's people unduly sensitive to criticism. They realize that they have done good work, under great strain, but when their financial situation is relieved they will be more disposed to co-operate. Queen's has done a great work and undoubtedly is entitled to provincial aid. The Western University, which many assert is not a university except in name, is evidently alive to the fact that the Carnegie Report disclosures cannot be ignored, and is showing more evidence of life and vigour than ever before.—Editorial, *Canadian Medical Association Journal*, 1: 361, April 1911.

SPECIAL ARTICLES

BLOOD BANKING
I. ABNORMAL ANTIBODIES AND THEIR DETECTION*

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R. C. HASSELBACK, M.D. and
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IN RECENT years there has been a steadily increasing demand for safely and rapidly cross-matched blood for use in hospitals across the country. Although many factors have influenced this trend, in large part it reflects the technical skills of surgeons and anesthetists, and the application to therapeutic medicine of such procedures as extracorporeal circulation. Fig. 1 shows the increased blood consumption and work load as seen at the Vancouver General Hospital over the past 10 years. The increased use of blood in 1958 and 1959 is almost entirely due to the institution of open heart surgery, while the sharp increase in the volume of blood cross-matched coincides with the opening of the hospital blood bank in September 1957 and the taking over of cross-matching from the Red Cross Blood Transfusion Service. The increased number of cross-matches represents not only the greater ease with which blood may be ordered and held in the hospital as a protective measure without an actual increase in utilization, but also reflects the number of repeat tests where difficulty is encountered in cross-matching. Coupled with the increasing surgical skills, rapid progress has been made in the knowledge of blood grouping factors and techniques. As the hazards of unmatched or inadequately matched blood have become known, so the need for rapid but safe techniques has become of paramount importance to the laboratory. One of the major problems facing the laboratory in its attempt to provide this service is the detection of abnormal antibodies in the serum of the recipient. This paper is a review of the experience with this and associated problems encountered at the Vancouver General Hospital blood bank over the past two and a half years.

Of equal importance are the organization and training of personnel for the blood bank. A second paper will review experiences with these aspects of blood banking.

METHODS

In the routine cross-matching procedure, the ABO grouping of the recipient was determined by both cell and serum settling techniques, while the Rh (D) typing was determined formerly by a saline anti D, and latterly by both saline and albumin anti D settling techniques. The cross-match was performed using saline at 20° C., albumin and indirect Coombs' (I.D.C.) tests at 37° C., with saline and albumin controls. The rapid cross-match method utilized a tile ABO and slide Rh (D) which were later checked by tube techniques. Spin techniques were employed with the saline, albumin, I.D.C. cross-match tubes. The donor blood was received from the Canadian Red Cross Blood Transfusion Service, where the ABO and Rh groupings as well as screening by Low's papain had been determined. Rh-negative blood was that found to be negative on testing with anti C, D, and E.

The antibodies detected on cross-matching were all investigated by saline, at 20° C. and 37° C., albumin and indirect Coombs' tests against a panel of cells of known genotype. Similarly, transfusion reactions were all investigated by complete recross-matching using both the pre- and post-transfusion specimens and by indirect Coombs' testing against a panel of cells using the post-transfusion specimen.

RESULTS

Since all cases in which abnormal antibodies had been detected during the 2½-year study had been carefully recorded, an analysis of this group was undertaken. Cases of erythroblastosis were excluded from this group and were considered separately. Over the study period 16,133 patients had been cross-matched, of whom 9300 received 33,504 bottles of blood. Of the 16,133 patients, 94 had been discovered to have 109 antibodies.* There were 80 patients with one, 13 with two and 1 with three abnormal antibodies. This gave an incidence of 0.58% for the overall recipient population, as compared with 0.16% found in the donor population at the Red Cross Transfusion Depot in Vancouver.[1] The distributions of these antibodies and their reaction are seen in Table I.

It is interesting to note that Lewis, Duffy and Kell antibodies together constituted approximately 40% of the total group. The Kell antibodies are particularly noteworthy in that their actual frequency is considerably higher than that detected, owing to the low incidence of the K antigen. In view of their importance in causing both hemolytic transfusion reactions and hemolytic disease of the newborn, Kell-negative blood probably should be given to all women of child-bearing age.

The high frequency of anti D antibodies detected was also surprising, as those found in the course of investigating cases of erythroblastosis were excluded, and it had been the policy to administer

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*The majority of sera were sent to the Canadian Red Cross Blood Transfusion Service or the Ortho Research Foundation for confirmation of antibody identification.

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TABLE I.

Antibody		Reactions of antibody: Sal. 20°	Sal. 37°	Alb.	I.D.C.	Other antibodies present in serum
Anti D (21)	1	—	—	+	+	
	2	—	—	+	+	Anti Fy[a]
	3	—	+	+	+	Anti C
	4	—	—	+	+	
	5	—	—	+	+	Anti C
	6	—	(+)	+	+	
	7	—	—	+	+	
	8	—	—	+	+	Anti Fy[a]
	9	+	+	+	+	Anti Jk[a]
	10	—	—	—	+	
	11	+	+	+	+	Anti P
	12	—	—	+	+	
	13	—	—	—	+	Anti C
	14	—	—	—	+	
	15	—	+	+	+	Anti E
	16	—	(+)	+	+	
	17	+	+	+	+	
	18	—	—	+	+	Anti C
	19	—	—	—	+	
	20	—	—	+	+	
	21	—	—	+	+	
Anti E (10)	1	+	+	+	+	
	2	—	—	—	+	
	3	+	+	+	+	Anti c
	4	—	—	—	+	
	5	—	+	+	+	
	6	(+)	+	+	+	
	7	—	+	+	+	Anti D
	8	—	—	+	+	
	9	—	—	+	+	
	10	+	+	+	+	Anti Fy[a] and K
Anti C (4)	1	—	+	+	+	Anti D
	2	—	—	+	+	Anti D
	3	—	—	—	+	Anti D
	4	—	—	+	+	Anti D
Anti c (3)	1	—	—	+	+	
	2	—	—	+	+	Anti E
	3	—	—	+	+	Anti Fy[a]
Anti A_1 (13)	1	+	—	—	—	
	2	+	—	—	—	
	3	+	—	—	—	
	4	+	—	—	—	
	5	+	+	(+)	—	
	6	+	—	—	—	
	7	—	—	—	+	
	8	+	—	—	—	
	9	+	—	—	+	
	10	+	—	—	—	
	11	+	—	—	—	
	12	+	+	+	+	
	13	+	—	—	—	
Unidentified (4)	1	—	—	—	+	
	2	—	—	—	+	
	3	—	—	—	+	
	4	+	—	—	—	

Antibody		Reactions of antibody: Sal. 20°	Sal. 37°	Alb.	I.D.C.	Other antibodies present in serum
Anti Lewis (16)	1	—	+	+	+	
	2	—	—	—	+	
	3	+	+	+	+	
	4	+	—	—	—	
	5	—	(+)	(+)	(+)	
	6	+	+	+	+	
	7	+	+	+	+	
	8	+	+	+	+	
	9	+	+	+	+	
	10	+	+	—	+	
	11	+	+	+	+	Anti K
	12	+	—	—	—	
	13	+	—	—	—	
	14	+	—	—	+	
	15	+	+	+	+	
	16	+	+	+	+	
Anti Duffy (15)	1	—	—	—	+	
	2	—	—	—	+	
	3	—	—	+	+	Anti D
	4	—	—	—	+	
	5	+	+	+	+	
	6	—	—	—	+	Anti K
	7	—	—	—	+	
	8	—	—	—	+	
	9	—	—	—	+	Anti K
	10	—	—	—	+	
	11	—	—	—	+	Anti c
	12	—	—	—	+	
	13	—	—	—	+	
	14	—	—	—	+	Anti D
	15	+	+	+	+	Anti E and K
Anti Kell (13)	1	—	—	—	+	
	2	—	—	—	+	
	3	+	+	+	+	
	4	(+)	+	(+)	+	
	5	+	+	+	+	
	6	(+)	(+)	(+)	+	
	7	+	+	+	+	Anti E and Fy[a]
	8	—	—	—	+	
	9	(+)	(+)	(+)	+	
	10	+	+	+	+	
	11	—	—	—	+	
	12	—	—	—	+	Anti Fy[a]
	13	+	+	+	+	Anti Le[a]
Anti P (6)	1	+	—	—	—	
	2	+	—	—	—	
	3	+	—	—	—	
	4	+	(+)	(+)	—	
	5	+	—	—	—	
	6	+	+	+	+	
Anti Kidd		—	—	—	+	Anti D
Anti M		+	(+)	(+)	—	
Anti H or O		+	—	—	—	
Anti H		+	—	—	—	

(+) Inconsistent weak positive reaction.

Rh (D) specific blood to all patients except to elderly male patients in times of blood shortage. Under these conditions their production seemed unusual, and a survey was made in an attempt to determine how the antibody was discovered. Of the 21 cases, eight were detected during investigation of 360 febrile and allergic transfusion or plasma reactions and another eight were found owing to difficulty in cross-matching. In five of these cases the incompatibility was due to an associated antibody other than the anti D; in three cases the antibody was found when positive blood was to be administered to adult Rh-negative males owing to a blood shortage. The remaining five cases were reported by the physician ordering blood as patients known to have this antibody.

In an attempt to define a truer incidence of abnormal antibodies among Vancouver General Hos-

pital patients requiring transfusion, and the role of transfusions and pregnancies in their production, the sera of 1168 consecutive recipients were screened for antibodies. Saline, bromelin, papain and indirect Coombs' tests were used, and the patients were all interviewed to determine their history with regard to previous pregnancies or transfusions. The results are shown in Table II.

Abnormal antibodies were found in 2% of the hospital population requiring transfusion. We were unable to determine how many of the Rh-negative males had received Rh-positive blood at a previous date, but the antibody production was obviously considerable.

and Coombs' complement test were negative. This was an incidence of 3% of the total number of babies examined, a figure which agreed closely with that reported in Hardyment's[3] study of inexplicable jaundice. In no instance did the addition of complement to the Coombs' test result in a positive reaction when the routine test was negative. Cases such as those described by Pollack must constitute a small proportion of the cases of unexplained neonatal jaundice.

Bromelin testing also added little to the survey; only one baby with a bilirubin of 19.8 mg. % on the third day, showed a positive bromelin test with a negative routine direct Coombs' test. The possi-

TABLE II.—ANTIBODIES FOUND ON SCREENING 1168 CONSECUTIVE RECIPIENTS

Sex and Rh	*Males Rh positive*			*Males Rh negative*			*Females Rh positive*			*Females Rh negative*			*Total*
Category	*NT*	*T*	*U*	*NT*	*T*	*U*	*NTP*	*TP*	*U*	*NTP*	*TP*	*U*	
Number of patients tested	201	100	122	43	15	37	80	309	143	13	79	26	1168
Number of patients with antibodies	—	3	—	—	6	—	—	2	1	—	11	1	24
Types of antibodies		1 P 1 Fy^a 1 K			1 P 4 D 1 Fy^a + D			1 E 1 H	1 K		11 D	1 D	

T = Transfused. NT = Never transfused. NTP = Never transfused or pregnant.
U = Unsatisfactory information.

It was not determined whether a transfusion or an erythroblastic pregnancy was the antigenic stimulus among the females.

Although complete records of cases of maternal sensitization during pregnancy were not available, there were records of exchange transfusions investigated during the 2½-year period under review. There was a total of 66 cases, of which 28 were due to Rh incompatibility and 13 to ABO (nine to anti A and four to anti B). Of the remaining 25 cases, although no abnormality was detected on testing, potential incompatibility of ABO or Rh (D) group between mother and child existed in nine. This left 16 cases with no satisfactory explanation for their jaundice. It was reported by Pollack[2] that some negative direct Coombs' tests found on the cord bloods of babies with hyperbilirubinemia would become positive with the addition of fresh human serum as a source of complement. A series of 500 unselected cord specimens was examined, using the method described by Pollack. The four donors used as a source of complement were of group AB with Le (a−b+) phenotypes, and all were secretors of A, B, H and Le^b substances.*

The specimens were also tested by the routine direct Coombs' procedure, and by bromelin. In the group of 500 infants tested, there were 53 whose bilirubin rose to 12 mg. % or over during their hospital stay. There were 15 jaundiced babies in whom no fetal-maternal ABO or Rh (D) incompatibility existed and in whom the Coombs' tests

bility of a weak anti D existed, but no reaction was obtained on testing the mother's serum against a panel of cells with bromelin. There were also six patients in whom repeatedly positive reactions with bromelin occurred, and in whom no possibility of ABO or Rh (D) incompatibility existed. On testing both mothers' and infants' specimens with Coombs' and bromelin against a panel, no antibody could be identified. Similarly six repeatedly positive reactions were detected while screening the 1168 recipients with bromelin. Two of these were due to rouleaux formation which could be readily identified as such in the other test media, but which gave definite agglutination in the bromelin tubes. The other four sera did not give any reaction in the other test media, either at 20° C. or 37° C., yet they gave consistently positive results with bromelin against the entire panel of cells. Although reliable in detecting Rh and saline antibodies, the bromelin method was unreliable in detecting Kell and Duffy antibodies.

DISCUSSION

From the preceding data several points of interest and practical importance emerge. The first is the value of albumin tubes in the performance of routine and urgent cross-matching. It can be seen from Table I that these were unreliable in the routine procedure in that Duffy, Kell and Lewis antibodies were missed as well as a significant number of Rh antibodies. Thus in many instances the single indirect Coombs' test result is the only indication of an incompatibility. Clearly a further

*Kindly performed by Ortho Research Foundation, Raritan, New Jersey, U.S.A.

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tube in the cross-match that would aid in the detection of the above-mentioned antibodies would be of great value.

There is no doubt that enzyme techniques offer certain advantages. In particular, bromelin testing is a rapid, simple and apparently reliable method of detecting Rh and saline antibodies. It has proved, however, unreliable in our hands in detecting Kell and Duffy antibodies. As these constituted a significant proportion of the antibodies encountered when using Rh (D) specific blood, it would therefore not be a satisfactory procedure. Another technique which could play a useful part in the cross-match would be an indirect Coombs' and a saline test against a master tube, containing cells with most of the major antigens. The value of this test lies in the fact that the antibody status of the recipient's serum would be known should the need for future transfusion arise, and the clinician would be forewarned of the dangers of unmatched blood.

In our experience the indirect Coombs' test has been most reliable, producing consistent results after an incubation period of 15 minutes or one hour, as used in the quick-spin and routine procedures. In an attempt to speed up the release of blood on quick-spin matching, we have investigated the feasibility of a five-minute incubation period. Testing for 22 different antibodies, including D, P, Le^a, K, Fy^a, C and E by both methods, the 15-minute incubation period gave positive results in all instances. Although the five-minute test gave weaker results, only two antibodies were missed, a weak anti D and an anti Le^a. The failure to detect the anti Le^a might have been due to the fact that the sera had been stored in the deep freeze for a considerable period and no fresh complement was added to the test system. At present an urgent cross-match requires 20 minutes, the blood being released for transportation to the patient after a negative five-minute (sensitization) Coombs' and saline reading. The 15-minute (sensitization) Coombs' and saline tube is checked and the blood is recalled if any incompatibility should be detected. In addition, the ABO and Rh group of the patient is checked by routine settling technique.

Despite the possibility of missing the rare antibody by this procedure, it is safer than the use of unmatched blood. As the blood is so quickly available, it obviates the need for unmatched blood in most cases. If the clinician could not wait for this short period, a rapid ABO and Rh (D) type could be obtained so that group and type specific blood might be administered. This method has another advantage in that O-negative hemolysin-free unmatched blood is conserved, and the need to give Rh-positive blood in emergency in time of shortage is greatly decreased.

To date all the blood issued by the quick-spin technique has been grouped and D-typed by slide technique.* No error has been detected on subsequent tube testing, and our series now amounts to 1400 patients. This experience does not agree with that of Boorman and Dodd,[4] who report a 1 to 5% error in the ABO grouping and state that the slide Rh technique is so inaccurate that it should not be used.

One definite and one probable hemolytic reaction have occurred in the 2½ years. In one case a bottle of blood was incorrectly released from the blood bank and sent to the wrong patient. The doctor failed to note the mistake and administered the blood. The patient manifested symptoms of a hemolytic transfusion reaction after receiving 125 c.c. of blood and the transfusion was stopped. The patient recovered uneventfully. A second probable hemolytic reaction occurred in an elderly male who received 27 transfusions over a 12-day period.

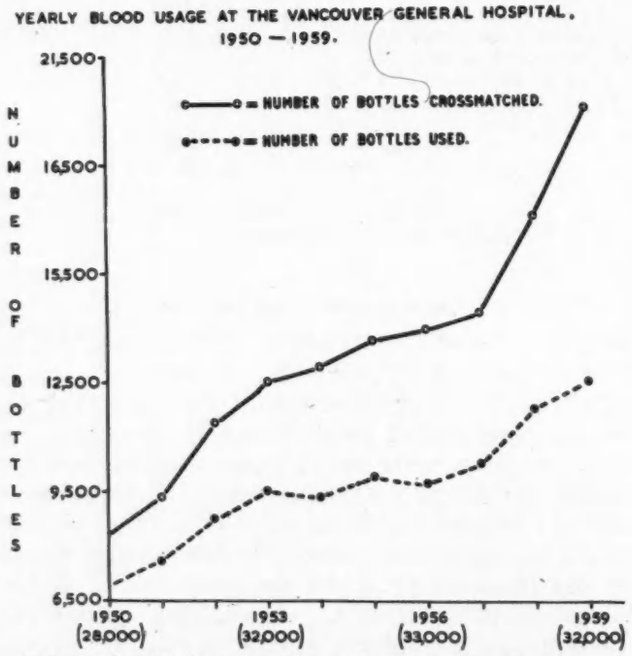

Fig. 1

During a three-day interim the patient's condition was so poor that specimens could not be obtained for cross-matching the subsequent bottles. They were matched with an earlier specimen. A reaction occurred to the contents of one of these bottles. Investigation revealed that an anti Fy^a apparently had developed as shown in the post-transfusion specimen. Presumably the first bottles acted as an antigenic stimulus, the titre being raised in the interval between transfusions. From time to time it will be difficult to obtain fresh specimens (less than 24 hours old) for cross-matching but every effort should be made to do so. Where large amounts of blood are ordered and are not used within three days, the unused bottle should again be cross-matched with a fresh specimen from the patient.

*Ortho slide anti D serum: Canadian Red Cross Transfusion Service anti A and anti B.

SUMMARY

While the incidence of abnormal antibodies found on routine cross-matching and investigative procedures was 0.6%, the incidence in the general hospital population requiring transfusion was found to be 2.0%. The four most commonly encountered antibodies were anti D, anti Le^a, anti Fy^a and anti K. Unmatched group O Rh-negative blood would not necessarily be safe in the presence of the latter three antibodies. A 20-minute cross-match method using a five-minute (sensitization) indirect Coombs' and saline test should satisfy most urgent requirements for blood and replace the use of unmatched blood.

The albumin tube in the cross-match fails to aid in the detection of many important antibodies. A second indirect Coombs' (37° C.) and saline test (20° C.) using pooled panel cells is recommended for routine cross-matching, and a second indirect Coombs' test using donor's cells for emergency cross-matching.

Patients with one antibody frequently develop a second antibody and should be looked upon as "antibody producers". Blood for such patients should be repeatedly cross-matched and administered with caution.

The authors would like to thank Dr. Irwin Kuhn and Dr. Norman Wignall for their assistance.

REFERENCES

1. STOUT, T. D.: Personal communication.
2. POLLACK, W., REISS, A. M. AND TREACY, M.: *Vox sanguinis*, 3: 442, 1958.
3. HARDYMENT, A.: Incidence and etiology of severe hyperbilirubinemia of the newborn—to be published.
4. BOORMAN, K. E. AND DODD, B. E.: Introduction to blood group serology, Little, Brown & Company, Boston, 1957, p. 22 and p. 69.

THE INTEREST OF ORGANIZED MEDICINE IN TRAFFIC ACCIDENTS*

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THE CANADIAN Medical Association took special cognizance of the medical aspects of traffic accidents in 1954, after a conference on this subject had been convened the previous year in Montreal by Dr. Harold Elliott. Dr. Elliott and a group of physicians in Montreal had focused attention on the importance of this problem and had encouraged the C.M.A. to establish a committee on medical aspects of traffic accidents to deal with it. The C.M.A. formed such a committee and appointed Dr. Elliott as Chairman, in which position he served for five years until he was succeeded in 1959 by Dr. Wallace Troup of Ottawa.

It might reasonably be asked, "What can a committee do about this problem, and what might be the logical outcome of its activities in the C.M.A.?" In reply it must be stated first of all that the C.M.A. has a long history of accomplishment in the health and medical fields, in founding specialist societies and health organizations, and in encouraging governments to take action for the prevention or control of specific health problems. There are many notable examples of such action, particularly in the fields of cancer, rheumatism and arthritis, and heart disease.

The usual outcome of any committee activity should be to make some recommendations to the profession or the public or both. In the first instance, the recommendations are made to, and approved by the General Council of the C.M.A. After that they are referred to those concerned, such as the medical profession, governments, other health agencies, or the general public. For example, the Committee on Occupational Medicine produced a booklet last year entitled "Guiding Principles for the Provision of Occupational Health Services". This was duly processed through the committee and General Council and was then distributed. The demand for this booklet has been unprecedented, and has required at least two special printings.

In the field of traffic accidents, many medical problems have been considered by the committee.[1] Some of these will be reviewed and it will be indicated how the C.M.A. might assist in their solution. They have all been discussed and recommended by the committee over the past few years.

One of the most important needs in the field of traffic accidents is the definition of medical standards for drivers, including physical and mental requirements for licensing drivers. This would appear to be one of the chief contributions that might be made by the medical profession in the prevention and control of traffic accidents. We are all aware of the hazard caused by an alcoholic, an epileptic, a diabetic or someone suffering from a mental or physical disability, who has an attack while driving his car and runs amuck on the road, injuring himself, his passengers and innocent bystanders. These individuals create a problem for themselves and others, and should be protected for their own sake and that of the general public.

A review of provincial regulations on physical and mental standards indicates that few, if any, provincial governments have comprehensive medical standards which govern licensing to drive. Most require drivers to declare their disabilities when applying for a licence, and some provinces require drivers of a certain age, or those who have been involved in accidents, to submit to visual or other examinations. However, there are no existing physi-

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cal or mental standards which might be applied across the country. In most provinces, the motor vehicle legislation gives the registrar or commissioner of motor vehicles the power to refuse to grant a licence on medical grounds. He has either a medical board or a physician to advise him concerning any individual's fitness to drive. For the most part, private practitioners issue certificates of disability and the registrar and his medical advisers decide whether to grant a licence. The question arises as to the physician's responsibility in divulging confidential information about his patient. Ethically, he is responsible to his patient, but morally and as a good citizen, he may have a responsibility to divulge information for the public safety. It is better that the patient admit his disability, and that an impartial board rule on the case, rather than that his personal physician be placed in an awkward position. At the present time, licensing authorities acquire information about an individual's inability to drive from various sources including relatives, police, doctors, social workers, public health personnel, hospitals and interested citizens.

The government of British Columbia in cooperation with the B.C. division of the Canadian Medical Association has established a "Medical Guide for Physicians in Determining Fitness to Drive a Motor-vehicle". This guide covers the major fields of medicine which might affect driving and is intended to assist doctors in assessing the ability of their patients to drive. Patients are advised to report disabling conditions to the licensing authority on renewal of their driver's licence, the onus being placed on the patient, not the doctor. This guide suggests minimal physical and mental requirements applicable to certain disorders, and outlines general recommendations for others. For instance, British Columbia, like most other provinces, will license an epileptic if he has been free of seizures for two or more years. Diabetics under treatment may also be licensed, and of course amputees and paralytics can be licensed provided that proper control mechanisms are installed in their automobiles.

A few years ago the Center of Safety Education of New York University[2] carried out a survey of laws and regulations in various states in the U.S.A., and has summarized the physical and mental requirements for licensing drivers. It also convened a symposium of well-informed people in this field to obtain a consensus of views on various standards. This study covered such considerations as visual standards, hearing, amputations and/or disabled limbs, addiction to alcohol, narcotics and other drugs, and factors of age and mental and neurological disorders.

The survey showed that among the 51 states and jurisdictions surveyed, visual standards varied widely. Thirteen states had visual standards that were different for persons with glasses and for those without glasses, but all 51 jurisdictions refused to grant driving licences to alcoholics, other addicts, and those mentally ill.

After this study, the experts recommended a visual acuity of 20/40 in one eye, or a correction to that level if glasses were worn. Colour blindness was not considered a basis for refusing a licence, as it was recommended that the size, shape and position of traffic lights be standardized. Where there was loss of a limb, or paralysis, it was suggested that one arm should be acceptable if the lower extremities were normal, or the driver should have one normal leg and normal arms. Hearing standards were recommended, which included a set of test words to be spoken at a distance of five feet from the driver. The repetition of 50% of the test words constituted a satisfactory test. No specific recommendations were made for a number of other conditions, such as heart disease and rheumatic disorders, because of the wide difference of opinion involving acceptable standards for persons with such disabilities.

A study of this kind would be useful in Canada, where it could be reviewed by the C.M.A.'s Committee on Traffic Accidents, with a view to preparing minimum medical standards for provincial licensing authorities. A start in this direction has been provided by the Canadian Ophthalmological Society, which has recommended "Visual Standards for Motor Drivers". These were recommended by the C.M.A. committee and approved by the General Council in June 1960.

Since most work on medical standards has been related to the eyes and to visual requirements, it might be of interest to give an illustration of the difficulty of obtaining agreement on various medical standards.

In recent years, a survey[3] was carried out in the United States which showed that a few blind pensioners had been issued with licences to drive. When this was pointed out, the licensing authorities were quite concerned at the apparent negligence of their officials. However, an investigation showed that although licences had been granted to nearly blind persons, the driving record of these pensioners had been carefully followed up since they had received their licences. In the first instance, they had only been granted a licence because of their limited field of operation, and were required to drive a car to make a living. Although this example represents an extreme departure from recommended standards of visual acuity, it serves to illustrate the differences in thinking between those who propose a minimum acuity of 20/40 and those who cite well-documented cases where drivers with 20/200 vision operate safely with restricted driving privileges.

The American Association of Motor Vehicle Administrators has studied this subject intensively and has recommended a minimum visual standard of 20/40 in one eye, which is the same as that set by other authorities. However, these standards leave some leeway for those with lesser vision who might

be considered for a driver's licence if individual circumstances warranted. The report goes on to state that, aside from physical defects which may have a bearing on the issuing of licences, the administrator granting a licence must know what type of individual the applicant is; whether he will exercise judgment sufficient to compensate for his limitations; how much driving he will do and within what area; what his economic needs are insofar as they involve driving; what his driving record is; how he performed during his road test, and whether the visual deficiency is a recent development or whether he has learned to live with it. A satisfactory answer to these questions might permit the licensing authority to issue a restricted licence.

These are the kinds of questions the C.M.A. committee will have to consider when it attempts to provide minimum physical standards for licensing drivers in Canada. In the final analysis, it will be the responsibility of the provincial licensing authorities to interpret these standards with the assistance of their medical advisers. The best approach would seem to be the provision of a guide, such as was provided in British Columbia, as many borderline cases will have to be judged on their own merits, which take into consideration the various factors of attitude, performance record, and the extent of driving, mentioned above.

A second problem concerns the use of seat belts to reduce injuries sustained in accidents. Surveys have shown that fewer traffic injuries occur when seat belts are used. The difficulty is to persuade people to use them even though they are available in the car. Many people will not take the trouble to fasten the belt around them. The C.M.A. has recommended that seat belts be installed in all motor vehicles as standard equipment and that the public be educated to use them. There has been some resistance from the motor car industry in this regard, as there appears to be some technical difficulty in inserting the proper lugs or hooks in all vehicles. This gives rise to the question whether the public would be willing to pay a little more for the automobile with this additional safety feature. In the past, they have not been shown to be willing to pay extra for such safety devices.

According to studies carried out at Cornell University,[4] persons who use seat belts while driving are 35% to 60% safer than those without. The Cornell scientists estimate that if seat belts were widely used by the motoring public in the United States, 5000 lives would be saved each year merely by restraining passengers within the car in the event of an accident. Seat belts reduce the speed of the impact that kills and disables automobile occupants. It is the violence of the reduction in speed, not the speed itself, that kills. Thus even low speed collisions can produce high deceleration rates. Seat belts help to prevent injury by reducing the speed of impact. Even though the occupant's head hits the dashboard, the blow is not nearly so forceful if he is wearing a seat belt. This can mean the difference between a major and a minor injury. The support of the Canadian Highway Safety Conference in recommending this safety device would go a long way in persuading motor car manufacturers to install seat belts as standard equipment in passenger vehicles.

A third major medical problem lies in the psychological field. This refers to the attitude of the driver, particularly the young or teen-aged driver. In other words, what makes an otherwise pleasant fellow act like a "demon" behind the wheel? Although this is not a purely medical problem, the C.M.A. committee believes in the principle of driver education of teen-agers in view of the high accident rate among the young men of this group. It is recognized that the immaturity of teen-agers provides an attitude which is not conducive to a low traffic accident rate. However, a good deal of education could be accomplished in this regard.

Here again this recommendation is difficult to implement, because the inclusion of driver training in the educational curriculum would further congest the already crowded curriculum of secondary schools in Canada. It is also doubtful whether boards of education would receive this suggestion favourably. The most likely solution therefore is to provide driver training for teen-agers as an extra-curricular activity. It is of note that the Departments of Education and Transport of the Ontario Government have both agreed on this principle and are taking steps to expedite the driver training of secondary-school students.

Another major medical problem is the emergency treatment of injured persons. This entails good communications in the event of traffic accidents, and the availability of emergency facilities and trained personnel when the accident victim arrives at the hospital. Research studies in Cornwall, Ontario, and in other centres have shown that adequate treatment can be provided for injured persons as long as good communications exist between the ambulance, the hospital, the doctor, the police department and the telephone service. In Cornwall, a system has been established on a pilot-study basis where all concerned are advised immediately through the telephone service as soon as an accident is reported. This means that the ambulance arrives promptly at the scene of the accident, the hospital is prepared for the case, the doctor is present, and the police are informed. It is hoped that these studies will provide a pattern which can be applied to other communities and which no doubt will result in more efficient, adequate care for injured persons. In addition to providing for good communications, it is important that all small hospitals be organized and equipped to render immediate resuscitation to the injured, and, if necessary, to prepare them for transportation to larger centres. This again requires teamwork of all concerned, and good communications. Once a pattern has been established which appears to operate successfully,

it would be the duty of the medical profession to recommend its use to other centres and provinces.

Probably the most important item which requires attention is research into the causes of traffic accidents. The other items mentioned are straightforward and can be organized and developed through the co-operation and education of those concerned. Traffic accidents occur because of two main reasons, human or mechanical failures or both. The medical profession, in the past, has recommended that certain changes be made in the design of motor vehicles because of the prevalence of certain injuries that have resulted during accidents. Protective devices such as shatterproof windshields and padded dashboards have prevented many serious injuries. It is the human causes and errors, however, which are of greatest interest since they appear to cause most accidents. Judgment may be impaired by alcohol or drugs, some emotional upset or fatigue. The study of human behaviour as it affects driving would be a fertile field for medical research. What makes people act as they do when they get behind the wheel of an automobile? A great deal is known about this now in respect of alcohol, drugs and fatigue. The time of day, too, may be of significance, since we know that a high accident rate occurs in the late afternoon or early evening. No doubt anything that preoccupies a driver will have an effect on the accident rate as well.

In 1954, one of the first recommendations of the newly formed Committee on Traffic Accidents concerned the establishment of a Canadian Medical Traffic Accident Research Foundation to stimulate and conduct research in this field. This movement was sponsored by the Canadian Medical Association, the Royal College of Physicians and Surgeons of Canada, l'Association des Médecins de Langue Française du Canada, and the Canadian Bar Association. Since that time, a federal charter has been granted for the formation of a research foundation, but as yet no funds have been forthcoming to permit such studies. It is hoped that these funds will be available in the not too distant future to fulfil an important need in the traffic accident field.

The C.M.A. has developed a close liaison with the Canadian Highway Safety Council, which is the national safety organization in Canada primarily concerned with the prevention of traffic accidents through public education. The chairman of the medical advisory committee of the Highway Safety Council is Dr. Wallace Troup. In his dual capacity as chairman of the Safety Council's advisory committee as well as of the C.M.A.'s Committee on Medical Aspects of Traffic Accidents, he provides ideal liaison between these two groups. It is hoped that through the Highway Safety Council funds may soon be provided for medical research in traffic accidents.

It is evident that the medical profession, through the Canadian Medical Association, is making an important contribution in the field of traffic accidents by providing medical standards for drivers, by promoting medical research in this field, and by recommending to governments and other agencies various safety measures which may reduce injury and death from this cause. There are a large number of dedicated physicians in Canada who have given unstintingly of their time and have shown considerable interest in this problem. Through them the C.M.A. will continue to play its part in this important field of endeavour.

REFERENCES

1. Canadian Medical Association, Committee on the Medical Aspects of Traffic Accidents: *Canad. M. A. J.*, **83**: 506, 1960.
2. New York University Center for Safety Education: Physical and mental requirements for the driver's license, 1959.
3. KERRICK, J. C.: *J. Am. Optometric A.*, **32**: 224, 1960.
4. Canada, Department of National Health and Welfare, Occupational Health Division: Smart drivers use seat belts, *Occupational Health Bulletin*, 15: No. 8, 1960. Reprinted from *National Safety News*, May 1960.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Possibly too much is made of the machinery for the teaching of medicine, and too little of the teachers themselves. The writer of Bulletin 4 for the Carnegie Foundation for the Advancement of Teaching, that is, the one which deals with medical education in the United States and Canada, can scarcely contain his glee as he describes the equipment of the larger schools. Rather a neat case has been made upon the other side by *American Medicine*, where it is pointed out that Dr. Simon Flexner, brother of the writer of the Bulletin, is a graduate of one of those schools which is so utterly contemned; namely, the University of Louisville. According to the Bulletin, "Laboratory facilities are inadequate in appointments and teaching force for the thorough teaching of the fundamental sciences to so large a student body. It has a large, scattered plant, unequal to the strain which numbers put upon it . . . There are radical defects for which there is no cure in sight; the classes are unmanageably huge; the laboratories overcrowded and undermanned; clinical facilities, meagre at best, broken into bits in order to be distributed among the aggregated faculty. To carry the school at all, a large attendance is necessary; but a large attendance implies a low standard. The situation is thus practically dead-locked." The answer to this is that the University of Louisville, with all its theoretical imperfections, has sent forth a graduate of the eminence of Dr. Simon Flexner. In Canada, the Halifax Medical College has suffered a like condemnation. The answer is again the quality of the graduates. To give a specific instance, Dr. F. J. Shepherd, dean of the medical faculty of McGill University, who is even more eminent as anatomist and surgeon than Dr. Flexner is as a physician, made his first medical studies in Halifax.—Editorial comment, *Canadian Medical Association Journal*, 1: 166, April 1911.

CASE REPORTS

DUPLICATION OF THE ILEUM WITH ASSOCIATED VERTEBRAL DEFECT*

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DUPLICATIONS of the alimentary tract have been defined[1] as "spherical or elongated hollow structures possessing a coat of smooth muscle and lined by mucous membrane which may be like or unlike that of the parent viscus. In most instances, they are intimately attached to some portion of the alimentary tract and may be found at any level from the base of the tongue to the anus. They are more commonly found in relation to the small intestine, particularly the ileum, than to any other part of the gastrointestinal tract." Dohn and Povlsen[2] reviewed the literature and found that approximately 40% of published instances of duplication occurred in the ileum.

In duplication involving the ileum, the presenting signs and symptoms are usually those of partial bowel obstruction due to pressure by the duplication on adjacent intestine. Complete intestinal obstruction may ensue in a number of ways: by fecal impaction, by a volvulus initiated by the duplication or by occlusion of the mesenteric vessels, since the duplication lies between the layers of the mesentery. Signs, such as melena, anemia and shock, can occur owing to peptic ulceration involving gastric mucosa lining the duplication. Rupture of the duplication because of accumulation of mucoid secretions, causes peritonitis.[3-5]

Most observers agree that a high proportion of duplications are associated with other malformations, and the following case is no exception. Vertebral anomalies are often associated with intrathoracic duplications. In a series of 61 cases of mediastinal duplication, Fallon[5] found 18 instances of spina bifida, hemivertebra or infantile scoliosis. Ware and Conrad (1953) found that 18 out of 81 cases with intrathoracic duplications had spinal abnormalities.[6] There is no record of a vertebral anomaly associated with a purely intra-abdominal duplication. The following case is reported to show that the combination of intra-abdominal duplication and vertebral defects is possible.

K.K., a white infant girl, came to autopsy 20 days after birth. She was the product of an apparently normal full-term pregnancy in a healthy young primipara. The prenatal history was unremarkable, and neither parent can recall any case of congenital malformations in their families. Labour was uneventful, lasting approximately six hours; the baby presented by the vertex in a right occiput anterior position. The baby showed obvious deformities at birth with a right talipes equinovarus and a dislocation of the left knee joint. The abdomen was markedly distended and soft. The clinical impression on palpation of the abdomen was that the abdominal musculature was deficient and a moderately large soft mass was present on the right side. The infant's colour and cry were of good quality. A flat-plate roentgen examination (Fig. 1) of the abdomen was carried out on the first day of life and showed a globular body outline due to the bulging, flaccid abdomen and a soft tissue mass on the right side displacing the gas-containing bowel towards the midline. A vertebral defect consisting of hemivertebra at the T3-T4 level with associated rib changes was noted. An intravenous pyelogram taken 10 days later showed no abnormality in kidney outlines, calyceal structures, pelves or ureters. Urinalysis on two occasions was negative. The hemoglobin value on the 18th day of life was 10.4 g. %. Blood urea on one occasion was 15 mg. % and on another, two days before death, was 33 mg. %.

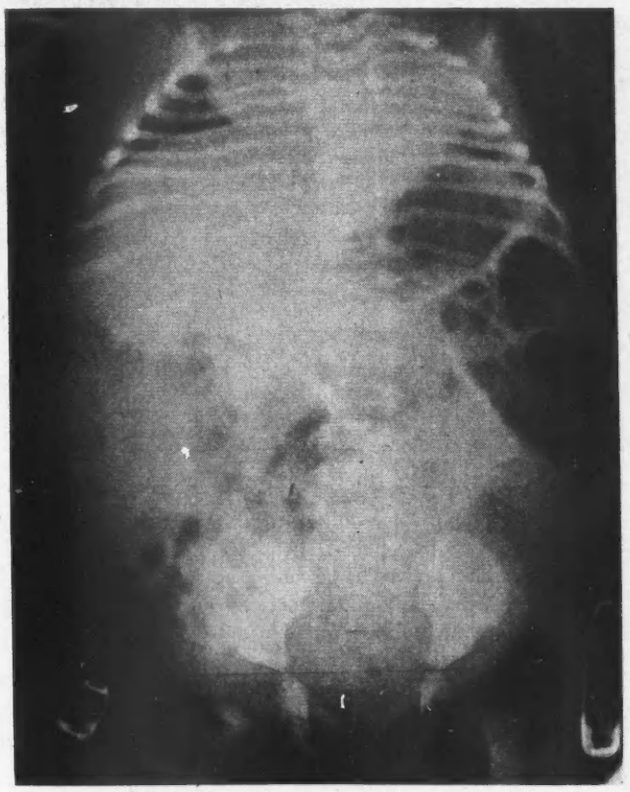

Fig. 1.—Roentgen examination performed on the first day of life showing the "globular" body outline; the presence of a soft tissue mass in the right abdomen, displacing the gas; and the vertebral defect at T3-4.

The baby was breast fed and given glucose by bottle. Feedings of moderate amount were tolerated till the 11th day of life when regurgitation became troublesome and intravenous therapy was begun. The bowel movements were scanty and remained mostly liquid until the 11th day of life, after which there were no bowel movements. At this time, the abdomen was grossly distended; enemas and gastric suction provided

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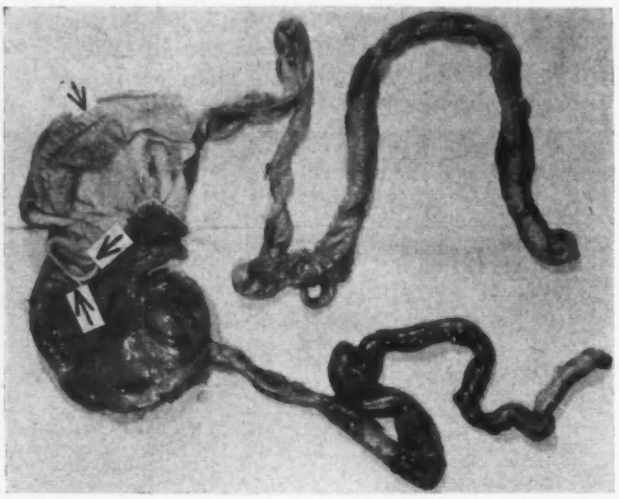

Fig. 2.—Photograph showing the large duplication intimately connected to the ileum. Half of the duplication and associated ileum are opened to show mucosal surfaces. The arrows indicate the lumen of the duplication and ileum seen on transverse section.

no relief. The baby's weight fluctuated from 7 lb. 15½ oz. at birth to 8 lb. on the 10th day and to 7 lb. 5 oz. on the last day of life. The baby became increasingly short of breath, pale and shocked, and the abdomen became more distended, these features terminating in death on the 20th day after birth.

At autopsy the body weighed 7 lb. 8 oz. and measured 48 cm., crown-to-heel length. The body was globular, measuring 41 cm. in circumference at the level of the umbilicus and 31 cm. at the level of the nipples. The peritoneal cavity contained 300 ml. of old and recent fluid and clotted blood. A large duplication, measuring 8 x 17 cm., was intimately attached to the medial border of a segment of ileum 34 cm. proximal to the ileocecal valve (Fig. 2). The duplication was on the right side of the abdomen, extending from the pelvic brim to the liver. An area of discolouration covered with recent blood clot was present on the posterior inferior wall of the duplication where rupture had taken place (Fig. 3). A disrupted mesenteric vessel in this area was the source of the intraperitoneal hemorrhage. On section, the ileum and duplication had a common serosal covering and separate lumens. The duplication was lined by flattened, atrophic mucosa and contained thick, stringy mucus mixed with fecal material. There was communication at three points where rupture had allowed intermixing of the ileal and duplication contents. Histological study (Fig. 4) shows that both ileum and duplication have complete mucosal, submucosal and circular muscle layers. The longitudinal muscle layer is deficient in an area where the ileum and duplication are joined and the circular muscle layers of both structures lie side by side. The mucosal lining of the duplication is atrophic and autolyzed. However, the presence of large cells with pale eosinophilic cytoplasm and round discrete nuclei suggests parietal cells of gastric mucosa.

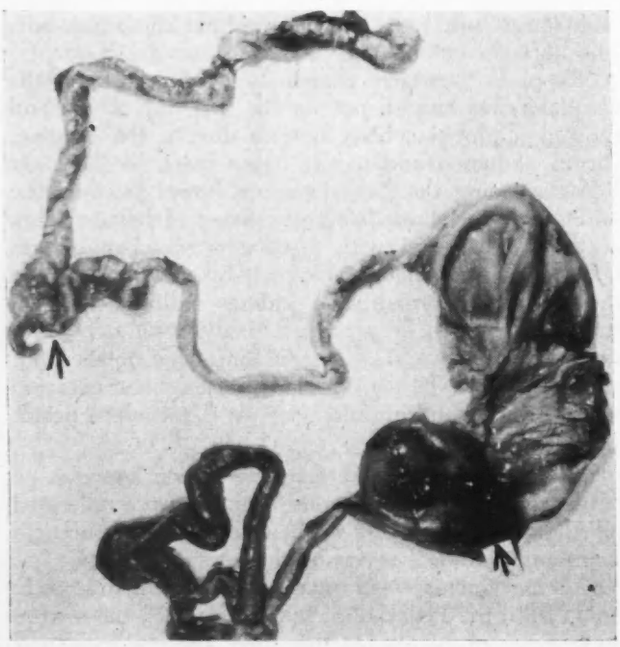

Fig. 3.—Photograph showing the posterior aspect of the duplication and the site of rupture and hemorrhage.

Fig. 4.—Low-power photomicrograph (x 2) showing relationship and size of duplication compared with normal ileum. (The small ileum lies on top of the duplication.)

SUMMARY

A case of pure intra-abdominal duplication of the ileum associated with vertebral skeletal defects is presented, a combination not heretofore recorded in the literature.

REFERENCES

1. GROSS, R. E.: The surgery of infancy and childhood, W. B. Saunders Company, Philadelphia, 1953, p. 221.
2. DOHN, K. AND POVLSEN, O.: *Acta chir. scandinav.*, **102**: 21, 1951.
3. BASU, R., FORSHALL, I. AND RICKHAM, P. P.: *Brit. J. Surg.*, **47**: 477, 1960.
4. BOYD, H. AND RUBINOW, M. B.: *J. Pediat.*, **49**: 326, 1956.
5. FECHER, M. P., DAY, S. M. AND KING, F. G.: *Ann. Surg.*, **135**: 555, 1952; correction **135**: 754, 1952.
6. FALLON, M., GORDON, A. R. G. AND LENDRUM, A. C.: *Brit. J. Surg.*, **41**: 520, 1954.
7. WARE, G. W. AND CONRAD, H. A.: *Am. J. Surg.*, **86**: 264, 1953.

"The experience of foreign countries seems to indicate that the midwife, even when licensed and controlled, is always a source of possible danger to the community. The same is true in the United States. A recent investigation in Ohio, for instance, showed that over fifty per cent. of the midwives practising there use no prophylactic measure against ophthalmia neonatorum. The essential inconsistency of simultaneous practice in a community by obstetricians and by midwives is that it involves a divided responsibility and a double standard of efficiency."—*The Boston Medical and Surgical Journal;* quoted in the *Canadian Medical Association Journal,* 1: 343, April 1911.

HEMANGIOMA WITH THROMBOCYTOPENIA*

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THE STRANGE and, as yet, unexplained combination of hemangioma and thrombocytopenia is a syndrome that is quite uncommon. Between the first report by Kasabach and Merritt[1] in 1940 and the most recent report of Gilon, Ramot and Sheba[2] in 1959, 14 cases have been described. If one is familiar with the syndrome, the diagnosis is simple. If one is unaware of the clinical picture, the diagnosis is not immediately obvious. This paper once again draws attention to this striking entity.

This 6-week-old baby boy was first seen on November 23, 1959, in consultation. For five days the mother had noticed a discolouration of the skin of the left side of the chest, which she thought was a bruise. Four days later, a definite swelling appeared in the centre of this discoloured area. The baby appeared to be otherwise in perfect health, but there was staining of the skin, resembling a bruise, extending from the left sternal border to the posterior axillary line from the level of the fourth to the seventh ribs. In the centre of this discoloured area there was a firm, apparently painless swelling, approximately hemispherical in shape and about 3 cm. in diameter. It was felt that this was a hematoma and that the baby must have unwittingly been injured. A radiograph on November 23 showed the soft tissue swelling, with perhaps a very slight extension of the mass into the left thoracic cavity. No further investigations were undertaken at this time.

During the next week the discolouration around the central lump faded, but the localized swelling remained. At the end of this period the surrounding discolouration again appeared. The central lump seemed rather larger and tender, but the baby himself appeared very well. He was admitted to hospital for investigation.

Further clinical examination revealed no other abnormality; in particular, there was no enlargement of the liver, spleen or lymph nodes. The baby did not look pale and there were no purpuric spots or petechiae. Capillary fragility was normal. Coagulation time (Lee and White) was normal. Bleeding time also was normal. Hemoglobin value was 11.2 g. %, with slight hypochromia. The leukocyte count was 9800 per c.mm., of which 42% were neutrophils, 56% lymphocytes and 2% monocytes. The platelet count was 80,000 per c.mm. The next day the platelet count was 72,000 and it remained between 30,000 and 80,000 per c.mm. until the abrupt rise which started on January 28, 1960, two months after admission (Fig. 3). A bone marrow biopsy revealed plentiful megakaryocytes and a normal marrow.

During the first week in hospital the bruising around the central swelling became more obvious and numerous tiny petechial hemorrhages appeared over the whole discoloured area (Fig. 1). The appearance

Fig. 1.—Numerous tiny petechial hemorrhages are present over discoloured area.

was most striking, and closely resembled that so dramatically illustrated by Rhodes and Borrelli.[3] Two tiny petechiae were also seen on the forehead and on the trunk, but capillary fragility was not increased, as estimated by the tourniquet test. The bleeding time was six minutes. Needle aspiration of the central lump produced no material for examination. A further radiograph of the chest, 10 days after the first film, showed some increase in the size of the soft tissue mass and a definite encroachment of the mass within the chest (Fig. 2). This resembled a localized pleural effusion or empyema. In addition, irregularity and mottling of the 8th and 9th ribs had become evident.

It was thought that the baby had "idiopathic" thrombocytopenic purpura with formation of a hematoma. The baby was given 5 mg. of prednisone twice daily for two days, the dose then being reduced to

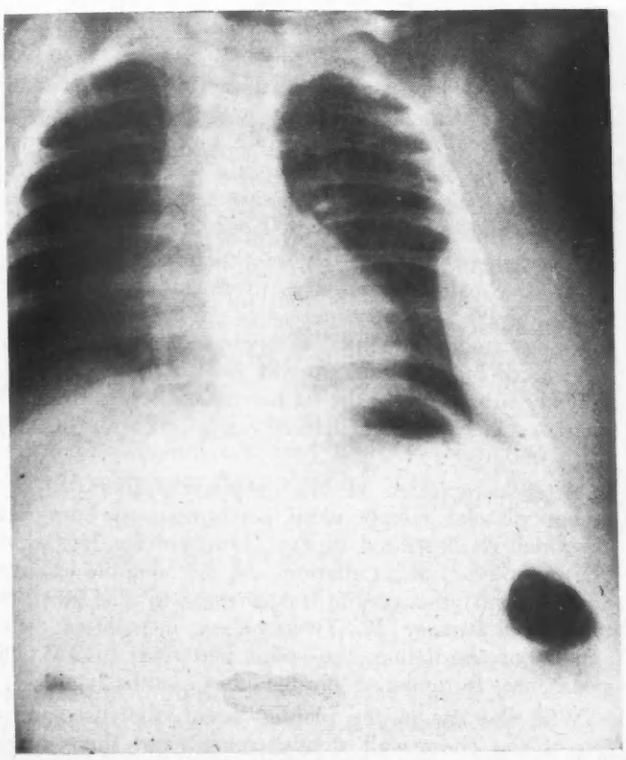

Fig. 2.—Chest radiograph, 10 days after the first film, showing some increase in the size of the soft tissue mass and a definite encroachment of the mass within the chest.

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2.5 mg. twice daily. After six days when there had been no response, the dose was increased to 5 mg. four times daily. Again no effect on the platelet count was noted.

Because another infant had previously been seen with thrombocytopenic purpura who had failed to respond to corticosteroids but had responded to ACTH, corticotrophin (Duractone) was given in a dose of 10 mg. daily for three days and 5 mg. daily thereafter. The dose of prednisone was gradually reduced and stopped. There was no response to corticotrophin.

On December 15, a biopsy was performed with considerable trepidation, for it was feared that there might be considerable bleeding. Freshly donated whole blood was in immediate readiness and a cut-down intravenous drip was running at the time of operation. These precautions were fully justified. An extremely vascular tumour was encountered. There was considerable blood loss and difficulty with hemostasis, but with arm pressure and transfusion of fresh blood the hemorrhage was controlled. A few fragments of pinkish-grey material were obtained. Histologically this was found to be, for the most part, hematoma undergoing organization. At the edge of the hematoma, however, there were cellular elements forming small capillaries. There was proliferation of these endothelial cells about and into the lumina of these capillaries. An occasional mitotic figure could be recognized. It was judged that this was a benign infantile type of hemangioma. It was now clear that we were dealing with the syndrome of hemangioma with thrombocytopenia as first described by Kasabach and Merritt in 1940.[1]

Two weeks after the biopsy, when the wound had healed, radiation therapy was started. At this time there was a deep purplish-brown discolouration of the left chest wall, extending from the sternum in front to the posterior axillary line posteriorly, and from the costal margin to above the left nipple. In the centre of this discoloured area there was a firm solid subcutaneous mass measuring about 8 cm. in maximum diameter, elevated about 3.5 cm. from the chest wall. There was a bruise on the right lower leg and extravasation of blood subcutaneously at the site of the cut-down incision and at the site of the venipunctures. The platelet count was 80,000 per c.mm.

Only the central portion of the tumour was irradiated. A cobalt-60 beam was used, giving eight treatments of 200 r over a period of 12 days. At the end of this time a definite erythema of the skin had appeared, but the tumour was smaller. The erythema quickly subsided and the tumour continued to diminish in size. No further irradiation was given after January 11, 1960.

After completion of the irradiation therapy, frequent platelet counts were performed, the progress of which is illustrated in Fig. 3. Seventeen days after the completion of irradiation, the first definite change was evident, the count having risen to 134,000 per c.mm. on January 28. Twenty-three days after completion of irradiation, the count had risen to 233,000 per c.mm. It remained normal nine months later.

With the rise in the platelet count, the discolouration of the chest wall slowly cleared and there were no further ecchymoses at the sites of venipuncture. Six weeks after the completion of radiotherapy, the

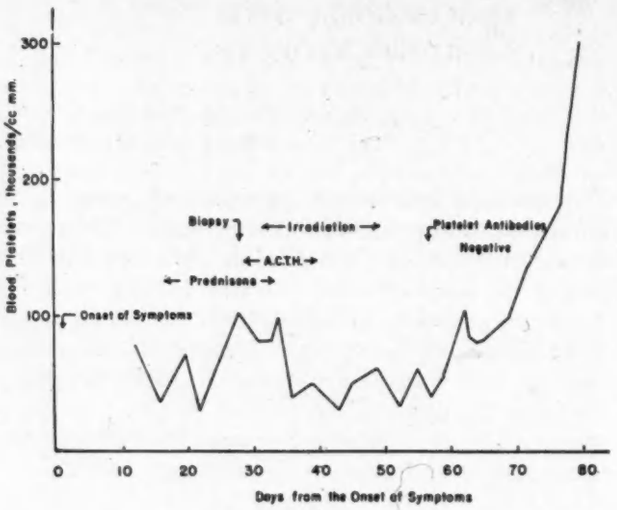

Fig. 3

tumour had shrunk so that it was 2.5 cm. in diameter and 1 cm. in thickness. Regression in size continued so that within three months the tumour had entirely disappeared. There remained only the scar of the biopsy. Along with regression of the external tumour, there was regression of the density within the thoracic cavity as shown radiologically. One year after the onset of this unusual condition, the baby is normal in all respects.

The sera of both mother and baby were examined for platelet antibodies (by Dr. J. L. Tullis) on the 57th day after the onset of symptoms, eight days after the completion of irradiation, and 15 days before the spectacular rise in platelet count. No such antibodies were found.

DISCUSSION

The similarity between the previously reported cases is striking. With the exception of the case of Gilon *et al.*,[2] all cases have first shown symptoms within the first few days or weeks of life. The bruised and purpuric area surrounding a more or less well-defined tumour is the presenting feature. Fluctuation in the intensity of the bruising and variation in the size of the discoloured area are quite usual. The common site of the hemangioma and surrounding ecchymosis is the upper trunk and neck. It is the predilection for this latter site that leads to danger, since, as reported by Franklin and Williamson,[4] compression and obstruction of the airway may result from enlargement of the hemangioma and hematoma.

This case throws no definite light on the cause of the thrombocytopenia. It has been suggested by Good *et al.*[5] that the platelet count is reduced by abstraction of platelets from the circulation and their utilization, in the hemangioma.

In this case one could scarcely doubt that in some way the hemangioma was either destroying platelets in the circulation or gathering them unto itself. But no platelet antibodies were found and no excessive accumulation of platelets was seen in the biopsy specimen. Nevertheless in this case, and in other cases, irradiation of the hemangioma led

to reduction in its size; and reduction in size was associated with a return of the platelet count to normal.

Gilon *et al.*[2] carried out careful investigations of the clotting mechanisms and platelet function in a 13-year-old child with multiple hemangiomas and thrombocytopenia. Their discovery of a qualitative platelet deficiency, a thromboasthenia, adds further confusion to our understanding of this bizarre syndrome.

Happily the prognosis seems to be good, the condition rapidly improving with irradiation of the hemangioma. It should be emphasized that biopsy must be approached with caution and no attempt made to remove the hemangioma. Hemorrhage at the biopsy site caused anxiety in the case reported here, and removal of the tumour in the case of Gilon *et al.*[2] required transfusion of 50 pints of blood.

SUMMARY

The fifteenth reported case of hemangioma with thrombocytopenia is described. Attention is again drawn to this bizarre yet characteristic syndrome.

Thanks are due Dr. Eunice McKishnie of West Lorne, who referred this patient to me, and to many others who assisted me.

REFERENCES

1. KASABACH, H. H. AND MERRITT, K. K.: *Am. J. Dis. Child.*, 59: 1063, 1940.
2. GILON, E., RAMOT, B. AND SHEBA, C.: *Blood*, 14: 74, 1959.
3. RHODES, A. W. AND BORRELLI, F. J.: *Am. J. Roentgenol.*, 52: 323, 1944.
4. FRANKLIN, A. W. AND WILLIAMSON, D. A. J.: *Arch. Dis. Childhood*, 28: 490, 1953.
5. GOOD, T. A., CARNAZZO, S. F. AND GOOD, R. A.: *A.M.A. Am. J. Dis. Child.*, 90: 260, 1955.

SHORT COMMUNICATIONS

A SIMPLE TECHNIQUE FOR THE CULTIVATION OF ANAEROBES*

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AT PRESENT the most popular method for cultivation of anaerobes on solid media involves the use of glass or metal jars. Their employment in a small bacteriological laboratory is time-consuming and cumbersome. When material arrives after the jar has been set up, either the whole procedure has to be repeated or the material is left until the next day. Furthermore, this method induces a certain amount of reluctance on the part of the technical staff to use anaerobic culturing more freely as a routine procedure.

Review of the pertinent literature has shown that there are certain methods of production of an anaerobic environment that are worthy of further improvement. Among these methods are those employing a mixture of pyrogallic acid and alkali. According to Hall,[3] Buchner (1888) appears to have been the first to utilize the pyrogallic acid-alkali mixture for this purpose. He placed this mixture into a large stoppered tube together with a smaller tube containing inoculum in either liquid or solid media. Blucher,[1] McLeod[7] and Spray[10] devised special glass or porcelain containers to hold and mix pyrogallic acid and alkali.

Lentz,[5] Koch[4] and recently Carlquist[2] and Mossel *et al.*[8] placed the chemicals upon the surfaces of the inverted bottom halves of Petri dishes, covering them by the top halves containing inoculated agar. Plasticine or molten paraffin around the rims of the top parts produced airtight seals. The above methods, however, possess the following disadvantages: (1) There is a risk of contamination of the media by bactericidal chemicals. (2) They result in frequent soiling of the incubator, bench, clothing and hands. (3) The types of seals described are inconvenient to use.

In order to eliminate these disadvantages, one of us devised and tested a further modification.[6] This was based on the utilization of polythene bags which were sealed by an electric heat sealer after the inoculated plates and the chemicals were placed within them. Both the pyrogallic acid and alkali were used in aqueous solutions and were poured on to Seitz filter discs. However, continuous use of this method showed that it is wasteful, since the solution of pyrogallic acid loses a considerable amount of its activity upon storage. Furthermore, a more simple and efficient method of sealing the bags was subsequently devised.

MATERIALS AND METHOD

Materials required—(1) Dry powdered pyrogallic acid and a dispenser (ladle) to accommodate roughly 0.6 to 1.0 g. of powder. (2) 50% aqueous solution of anhydrous sodium carbonate (stored at 37°C.). (3) Polythene bags, approximately 10½" x 6" (colostomy bags: Stevens and Co.), cut down to 7" x 6". One of the sides to be cut ¼" to ½"

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Fig. 1.—Polythene bag with inoculated plate and indicator (far left corner) in place. A screw cup containing Seitz filter is ready to receive chemicals. Note that the shorter side of the bag is facing upwards.

shorter (Fig. 1). (4) Fine porosity Seitz filter discs, 35 mm. in diameter, and a small plastic or metal screw cup to accommodate them. (5) Roll of cellulose tape (¾″). (6) Eh indicator (B.B.L. Thioglycollate-resazurin broth of Pittman[9] incorporating 1.5% agar)[8] in a small glass cup (5 c.c.). (7) One dropping pipette marked at 2 c.c.

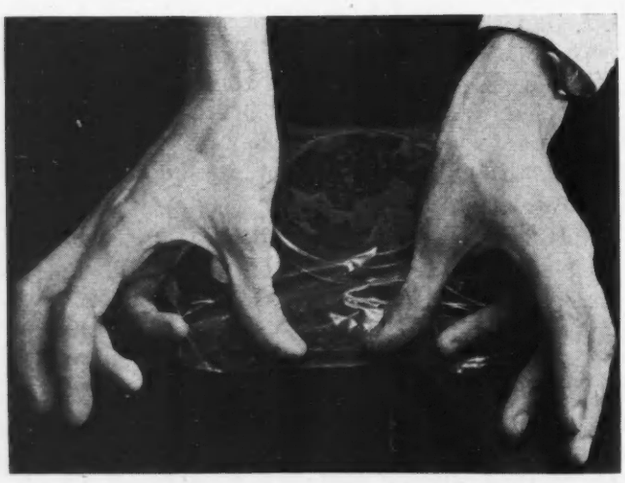

Fig. 2.—Cellulose tape is attached to both little fingers while the thumbs are placed centrally. Sealing begins from the centre of bag with an outward sliding motion of both thumbs. The centre of the tape should run along the edge of the short side of the bag.

Procedure—(1) Put into the polythene bag, placed with its shorter side up, an inoculated plate and Eh indicator. (2) Tear off a strip of cellulose tape approximately 7″ long. (3) Place on to the Seitz filter in a screw cup a ladleful of pyrogallic acid. (4) Pipette on to it 2 c.c. of alkali, put it into the bag and seal the latter immediately with cellulose tape as shown in Figs. 2 and 3. The assembly is now ready for incubation.

COMMENT

This method has been utilized for culturing *Cl. perfringens, Cl. tetani, Cl. sporogenes* and anaerobic streptococci, and has consistently produced good growth after an incubation period of 18 to 24 hours. The resazurin indicator changed from pink to yellow in about four hours and served well to show the development of the anaerobic state of the environment. The method was found to be fast, easy to use, clean and relatively inexpensive. It eliminated all of the disadvantages of previously described methods, especially the risk of contamination or soiling of the incubator, bench and hands by organisms or chemicals. Furthermore, material can be put up for culture when it arrives at the very end of the working day as well as at night.

Fig. 3.—The seal is completed by attaching the free ends of cellulose tape to the opposite side of the bag.

Production of a CO_2 environment is also possible by utilization of sodium carbonate and a weak solution of hydrochloric acid by adaptation of a similar technique. This is still in the process of testing.

The authors wish to express their gratitude to Dr. R. J. Gibbons, Professor of Bacteriology of the University of Ottawa, and to Dr. R. H. Allen, Chief, Clinical Laboratories, Department of National Health and Welfare, Laboratory of Hygiene, Ottawa, for supplying stock cultures of several anaerobes.

REFERENCES

1. BLUCHER, H.: cited in: *J. Bact.*, **17**: 255, 1929.
2. CARLQUIST, P. R.: *Am. J. Path.*, **35**: 273, 1959.
3. HALL, I. C.: *J. Bact.*, **17**: 255, 1929.
4. KOCH, F. E.: Cited in: *J. Path. & Bact.*, **78**: 290, 1959.
5. LENTZ, A.: Cited in: *J. Bact.*, **17**: 255, 1929.
6. MATTHEWS, A. D.: C.S.L.T. Thesis for specialty certification, May 1960.
7. MCLEOD, J. W.: *J. Path. & Bact.*, **17**: 454, 1913.
8. MOSSEL, D. A., GOLSTEIN BROUWERS, G. W. VON AND BRUIN, A. S. DE: *Ibid.*, **78**: 290, 1959.
9. PITTMAN, M.: Cited in: *Ibid.*, **78**: 290, 1959.
10. SPRAY, R. S.: *J. Lab. & Clin. Med.*, **16**: 203, 1930.

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A STUDY OF DEATHS IN CANADA ASCRIBED TO LUNG CANCER

A. J. PHILLIPS, Ph.D.,* *Toronto*

IN A previous paper[3] the author reviewed the mortality from lung cancer in Canada for the period 1931-1952 and showed that, in males, the age-adjusted death rates per 100,000 population had increased from 3.0 to 17.0 and in females from 1.6 to 3.7. Subsequent calculations for the years 1953-1958 show that, in males, the rate has increased to 26.3 but in females only to 3.8. For the period 1931-1958, then, lung cancer mortality rates in Canada have increased 8.8 times for males and 2.4 times for females. A later publication[4] studied these increases with reference to the possible effects of faulty certification of lung cancer deaths to other respiratory diseases, as proposed by Gilliam,[1] and the possibility of a change in diagnosis, as suggested by Herdan.[2] The results of this study showed that all of the increase in lung cancer mortality since 1931 could not be accounted for by erroneous death certification to other respiratory diseases and, also, that a diagnostic error of 5% would, theoretically, account for a major portion of the recorded increase. Thus, if 5% of the deaths attributed to respiratory diseases were actually due to lung cancer, the recorded increase in males since 1931 (8.8 times) would be reduced by over 50% and the increase in females (2.4 times) would completely disappear. The selection of an error factor of 5% was quite arbitrary, but its effect revealed the necessity for a study of the reliability of the diagnosis in deaths ascribed to respiratory diseases.

As a beginning it was decided to review the deaths due to cancer of the lung. A proposed outline of such an investigation was first presented to the Provincial Ministers and Deputy Ministers of Health at the Dominion Council of Health meeting in October 1958. The outline suggested that, for one year, deaths ascribed to primary lung cancer be referred back to the doctors responsible for the diagnosis with a request that they indicate whether or not the diagnosis was based on pathological, radiological, or clinical evidence. This proposal was accepted subject to the approval of the provincial medical associations. Such approval was subsequently obtained by the Deputy Ministers in their respective provinces.

The calendar year 1959 was selected for study in all provinces† except two; in Ontario the 12-month period June 1, 1959 to May 31, 1960 was chosen and in Newfoundland the calendar year 1956. All information relative to the identity of the cases has been considered confidential, and in some provinces the results of the analysis have been made known only to the writer. Where the diagnosis was based upon more than one type of evidence, pathological was selected over radiological or clinical, and radiological was selected over clinical. In the case of an autopsy the diagnosis was recorded as pathological.

The study includes 2235 deaths. The co-operation of the medical profession was nearly 100%; less than 25 deaths had to be excluded owing to the refusal of the doctor to provide data requested. The analysis of the 2235 cases shows that 72.1% were based on pathological evidence, 23.1% on radiological evidence and 4.8% on clinical evidence.

DISCUSSION

Statistical studies which derive their data from replies of individuals rarely attain total participation and it becomes necessary to interpret the results in the knowledge that they are based on something less than the whole. In many instances a 50 to 70% return has to be accepted. It should be stressed, therefore, that in the present study the excellent co-operation of the medical profession has resulted in a coverage of approximately 99% of all deaths from primary lung cancer in Canada in one year. Such a high degree of participation increases the reliability of the results of the inquiry.

The fact must be accepted that circumstances arise in which the doctor must rely solely on his clinical impression when making a diagnosis. In primary lung cancer the limitations resulting from such circumstances make an accurate diagnosis most difficult. The results of the present study, therefore, could be interpreted to indicate that the maximum diagnostic error in primary lung cancer is in the realm of 5%—this being the proportion of diagnoses based upon clinical evidence. However, such an interpretation assumes the improbable situation that all clinical diagnoses are incorrect. It is perhaps more accurate to estimate the diagnostic error as considerably below the 5% level.

SUMMARY

A one-year study has been made of the criteria used in the diagnosis of primary lung cancer in Canada.

The analysis shows that, of 2235 deaths, 72.1% were based on pathological evidence, 23.1% on radiological evidence and 4.8% on clinical evidence.

The study covers approximately 99% of all primary lung cancer deaths which occurred in Canada in the study year.

The National Cancer Institute of Canada wishes to acknowledge the assistance of the Provincial Ministers and Deputy Ministers of Health and the Provincial Medical Associations in this study.

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†The province of Prince Edward Island, population 102,000, was not included, as the annual number of deaths from lung cancer is less than 10.

REFERENCES

1. GILLIAM, A. G.: *Cancer*, 8: 1130, 1955.
2. HERDAN, G.: *Brit. J. Cancer*, 12: 492, 1958.
3. PHILLIPS, A. J.: *Canad. M. A. J.*, 71: 242, 1954.
4. *Idem*: *Brit. J. Cancer*, 13: 589, 1959.

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CURRENT CONCEPTS OF IMMUNOLOGY: IV. AUTOIMMUNE DISEASE IN MAN

THE PREVIOUS editorials in this series have outlined current concepts of the mechanism of immunologic homeostasis, that phenomenon by means of which the normal body is capable of recognizing and distinguishing between "self" components and foreign antigens. Occasionally this homeostatic mechanism may become deranged if mesenchymal cells are so changed by fortuitous mutations that they give rise to new generations of cells which proliferate and form "forbidden clones" of immunologically competent cells that are reactive to normal tissue components. These, upon interacting with parenchymal cells of a variety of target organs, lead to the development of specific autoimmune, or more accurately, autoclastic (self-destroying) diseases. Thus arose the concept that an organism has the inherent ability to develop antibodies to its own tissues and subsequently to destroy the structures containing the immunizing antigens.

There is an increasing body of both clinical and experimental data in support of this concept. It has now been demonstrated that injections of homologous brain tissue into animals results in the production of "allergic encephalomyelitis" which is accompanied by the presence in the blood, of circulating antibodies to brain tissues. Injection of testicular extracts together with Freund's adjuvant into rats and guinea pigs produces aspermatogenesis and circulating "antitesticular" antibodies. Similarly, injection of homologous thyroid extracts plus adjuvant in dogs, rabbits and guinea pigs is followed by the appearance of circulating antibodies to thyroid tissue as well as by histological changes in the thyroid gland. The suggestion that autoimmunization plays an etiological role in certain human diseases is supported by the demonstration of circulating antibodies to adrenal tissue in some patients with idiopathic Addison's disease; to sperm in occasional cases of orchitis; and to thyroglobulin or thyroid extract in many types of thyroid disease. Autoantibodies against a steadily growing list of other body tissue and organ components have also been shown to exist.

Recently, Burnet has classified the human autoimmune diseases in three main groups: (a) conditions due to immunologically based drug reactions, such as Sedormid purpura; (b) diseases due to immune reaction against a normally inaccessible antigen, e.g. Hashimoto's thyroiditis and idiopathic Addison's disease; and (c) autoimmune diseases directed against common body components, e.g. systemic lupus erythematosus and rheumatoid arthritis.

According to this concept, Sedormid acts as a hapten (i.e. an incomplete antigen) which is converted into a complete antigen by a loose union with platelets. When this antigen reacts with its antibody the result is platelet damage and purpura. A comparable mechanism is attributed to the hemolytic reactions to such drugs as quinidine and stibophen.

In recent years considerable research has been directed towards the investigation of Hashimoto's thyroiditis and other thyroid disorders associated with circulating antithyroid antibodies in the blood. By various techniques it has been demonstrated that there are two quite distinct types of thyroidal antigens, thyroglobulin and a microparticulate fraction of the cytoplasm of thyroid cells. Antibodies to both of these types of thyroidal antigen occur most frequently and in highest titre in patients with Hashimoto's thyroiditis or with the myxedema that follows it. Both may be present, however, in a high proportion of patients with any thyroid disease and in a small proportion of normal persons. Thus it appears that the antibody itself is not the primary *cause* of such diseases. It is generally believed that thyroglobulin and the cytoplasmic thyroid antigen are both specific to the thyroid and do not normally reach the general circulation. However, if inflammation or other disease processes within the gland permit escape of these antigens into the circulation they act as foreign moieties that give rise to antibody formation and to an immunologically modified population of lymphoid cells. This does not necessarily always result in thyroid lesions or gradual loss of thyroid function as occurs in patients with Hashimoto's disease. In autoimmune thyroid disease in general there is evidence that some pre-existing weakness of immunologic homeostasis is necessary to endow the immunologically modified lymphoid cells with the aggressiveness required before they can invade and multiply in the target tissue.

A wide variety of other disorders may be attributed to autoimmune disease in which the antigenic factors appear to be non-specialized components of body fluids and cells. Despite the reluctance of many clinicians to extend the concept of autoimmunity beyond those conditions in which antibodies against some specific body component can be

clearly demonstrated, there is an increasing trend to search for an autoimmune component in a broad range of subacute and chronic diseases of obscure etiology. It is important to recognize that the primary feature of such disorders is not an anomaly of antigens but a derangement of immunologically competent *cells* and of the homeostatic mechanism that should prevent the emergence and pathogenic activity of these cells and the antibodies they produce. Indeed there is some evidence that even antibodies are not necessarily of primary importance in the pathogenesis of such diseases, as indicated by the fact that an autoimmune disorder resembling rheumatoid arthritis is seen not infrequently in patients with agammaglobulinemia who are presumably incapable of manufacturing antibody.

In certain of the autoimmune diseases there are indications of a widespread breakdown in the mechanism of immunologic homeostasis. The most striking example of this is encountered in systemic lupus erythematosus in which a whole series of antibodies against common nuclear constituents, particularly desoxyribonucleic acid, can be demonstrated. Similar widespread failure of homeostasis is evident in rheumatoid arthritis. In this disease, as in any autoimmune condition associated with circulating antibody, the possibility exists that the gamma globulin of the antibody may become denatured, and in a person with inadequate homeostatic control this denatured gamma globulin may itself act as an antigen. In patients with rheumatoid arthritis the characteristic antigen involved in the well-known rheumatoid serologic phenomena is denatured gamma globulin. In acquired hemolytic anemia the most commonly encountered red cell antigen is apparently unrelated to any of the blood groups defined by natural or acquired isoagglutinins. It is a factor common to all human red cells and therefore is antigenically silent in all normal persons. Here, again, is demonstrated evidence of homeostatic breakdown of such a degree that it permits reaction with one of the most widespread human antigenic determinants.

There is also evidence in support of the view that certain clinical conditions such as rheumatic fever, acute glomerulonephritis and the benign hemolytic anemia that may follow infectious mononucleosis or viral pneumonia represent transient and potentially reversible autoimmune diseases. These disorders presumably result from a breakdown at some point of the homeostatic mechanism that is capable of reverting to normal after the initiating infection has subsided.

To recapitulate, it is postulated that in autoimmune diseases one is dealing with the emergence of a clone of immunologically competent cells which are not susceptible to the normal process of homeostatic control and that some of the conditions which bring about this state of affairs appear to be transitory and reversible.

An extensive report of the subject of autoimmune mechanisms of disease production by Doctors J. W. Steiner and R. Volpé will be published in an early issue of the Journal.

REFERENCES

1. Editorial: *Canad. M. A. J.*, **84**: 552, 1961.
2. *Idem*: *Ibid.*, **84**: 608, 1961.
3. *Idem*: *Ibid.*, **84**: 666, 1961.
4. BLIZZARD, R. M. AND CHANDLER, R. W.: *J. Pediat.*, **57**: 399, 1960.
5. BURNET, F. M.: *New England J. Med.*, **264**: 24, 1961.

TELEVISION EPILEPSY

IN THE past two decades there has been an obvious trend to attribute to the television set, responsibility for an increasing number of mankind's tribulations ranging from juvenile delinquency to the fast-draw syndrome (known in certain circles as "the Gunsmoke Gash"). The recent recognition of an entity known as "television epilepsy", therefore, should occasion no undue surprise or incredulity.

As early as Galen's time it was recognized that a seizure might be provoked by rotating a potter's wheel before the eyes of certain individuals. This observation was used by the slave traders of the day as a test for epilepsy in their prospective purchases and is probably the earliest reference to the epileptogenic potential of flickering light.[1] In the era of more modern medical history Gowers was among the first to recognize and document this phenomenon.[2] Subsequently it became apparent that there exists a certain group of epileptics who are sensitive to light, and in particular to flickering light. Such photic stimulation may, in certain subjects, induce any of the various clinical types of seizures, and indeed, some individuals of dubious moral standards have employed this phenomenon to bring on their own convulsions on occasions when this would be to their advantage.

Since 1952 a gradually increasing number of instances have been reported in which a television set provided the epileptogenic stimulus that triggered the onset of seizures in susceptible subjects.[3-8] The majority of these persons had a history of previously recognized epilepsy but in rare instances the initial or only fit experienced by the subject concerned, occurred in association with television viewing. Most of those affected have been children or young adults but "television epilepsy" has also been encountered in the middle-aged.

Despite the relatively high incidence of clinically recognizable epilepsy in the general population and the incidence of latent epilepsy which is presumably even higher, the number of cases that have been attributed to photic stimulation from a television set appears to be unusually small in view of the large numbers of susceptible persons who must be exposed to such a stimulus. This apparent discrepancy may be due in part to the fact that some cases of "television epilepsy" escape recognition, but it is probable that there are other reasons why

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the number of such cases that have been reported is so much smaller than might be expected.

It appears that the nature of the epileptogenic stimulus from the television set must be highly specific and that this stimulus must possess certain characteristics without which it will fail to evoke a seizure. Thus, although in nearly all cases described the subjects have been habitual televiewers, their epileptic manifestations did not occur unless they were exposed to a brightly illuminated, relatively slowly flickering screen at close proximity to their eyes, in a darkened room. Characteristic of the majority of such cases is the history of onset of the seizure while the patient was bending over the television set adjusting the controls and watching a flickering image on the screen.

Electroencephalographic studies on some of these patients confirmed that photic stimulation from a flickering source was associated with abnormal EEG patterns and sometimes with myoclonic jerking progressing to grand mal convulsions if the stimulus was continued over a sufficiently prolonged period. The flicker frequency usually required to induce these changes was in the range of three to 40 per second, and was usually between 18 and 30 per second. Apparent brightness of the flickering light is another factor of importance, the epileptogenic potential increasing with the proximity of the subject to the screen. In the majority of instances reported the patient was less than 45 inches from the screen when the seizure occurred. The degree of contrast in the intensity of illumination between that of the flickering source of light and that of the surrounding room is a further factor of significance. In one study it was demonstrated that the induction of the electroencephalographic and clinical manifestations of epilepsy by photic stimulation in patients with a history of "television seizures" was significantly facilitated by darkening the surrounding room. Conversely, when the same flickering light stimulus was applied in brighter surroundings, a longer period of exposure was required to induce epileptic manifestations.[6]

It has also been demonstrated in each case studied electroencephalographically that the susceptibility to all parameters of stimulation (i.e. distance from the source of flickering light, intensity of illumination of the source and surroundings, duration of stimulus and flicker frequency) is remarkably constant from day to day, and at various times throughout any one day.

In some patients the epileptogenic potential of flickering light is increased by closing the eyes; in others, the reverse of this finding has been described.

These observations constitute impressive evidence that television sets, particularly those functioning in a faulty manner, are powerful sources of photic stimulation. It seems obvious that epileptics who are sensitive to light should avoid this form of stimulus. The most effective way they can do this is to stop watching television, permanently. Since such advice is not likely to be followed, they should at least avoid watching a brightly illuminated screen in a darkened room, and should promptly divert their gaze from the screen if it starts to flicker. Under no circumstances should they approach a flickering screen or remain facing it with their eyes closed.

REFERENCES

1. TEMKIN, O.: The falling sickness, The Johns Hopkins University, First Series; Monographs, Vol. IV, Johns Hopkins Press, Baltimore, 1945.
2. GOWERS, W. R.: Epilepsy and other chronic convulsive diseases, J. & A. Churchill, London, 1881.
3. LIVINGSTON, S.: *Am. J. Dis. Child.*, **83**: 409, 1952.
4. KLAPETEK, J.: *Electroenceph. clin. Neurophysiol.*, **11**: 809, 1959.
5. WHITTY, C. W. M.: *Lancet*, **1**: 1207, 1960.
6. PALLIS, C. AND LOUIS, S.: *Ibid.*, **1**: 188, 1961.
7. MAWDSLEY, C.: *Ibid.*, **1**: 190, 1961.
8. Letters to the Editor: *Ibid.*, **1**: 394, 1961.

CANADIAN DOCTORS IN FRANCE

THE Association of Canadian Doctors in France was formed in 1948 under the sponsorship of "l'Association des Médecins de Langue Française du Canada", with the support of the Dean of the Faculty of Medicine in Paris and other prominent medical personalities in France. This organization serves Canadian doctors who are studying in Paris and other French medical centres, and has also arranged lectures by Canadian doctors in France.

In a special supplement of *La Revue du Practisien* (10 Supp.) No. 33, December 21, 1960), Georges Durand discusses the past, present and future plans of the Association and describes its activities in organizing trips to such centres as the great hospital city of Lille. A. Viallet, of the University of Montreal, and S. Richer, of McGill University, describe their personal experiences in Paris hospitals.

Although it was customary before the Second World War for French-speaking Canadian physicians to pursue their postgraduate studies in France, this practice has not been resumed to the same extent in the postwar period. The reasons for this are discussed by Durand, who appeals for efforts on the part of responsible authorities in France to influence Canadian doctors to resume the previous trend to carry out their postgraduate training in French universities and hospitals. Regular meetings of French Canadian and French groups have been organized in the past, the most recent of such meetings being the 11th National Congress of "France-Canada" which was held in Montagne on March 11 and 12 of this year. It is also planned to organize week-end trips to various historic sites and other places of interest, including the University of Caen, the restoration of which has been achieved largely as a result of Canadian generosity. Pilgrimages to Normandy are planned, to visit the beaches where so many Canadian soldiers fell during the war.

Information about the Association of Canadian doctors in France is published regularly by *l'Union Médicale du Canada*. W.G.

LETTERS TO THE EDITOR

STUDIES OF MALE SURVIVORS OF MYOCARDIAL INFARCTION

To the Editor:

May I seek the use of your columns to express my difference with Shanoff *et al.* (*Canad. M. A. J.*, 84: 519, 1961) concerning the naïve use of the term "heavy" for the consumption of three ounces of alcohol daily? I would not advance that my personal daily use of three times this amount should become the criterion except that the facility of my confrères to keep pace with me, when my guests, suggests that it is about average, unless I have only dissolute medical companions! I sincerely hope that this frankness will not lessen their readiness to accept my hospitality. The authors, I judge, may all be on the "proper" side of the maxim "Drinking is a luxury till forty and only later does it become a necessity." I would submit that the dosage of alcohol in their "heavy" drinking group is inadequate to effectively influence coronary vessels. I prefer to place "spiritus frumenti" high on the list of useful drugs if in proper dosage, especially for my own medicinal use, for I have a threatening history with a brother, father and paternal uncle all victims of coronary artery disease. Hastily I would add that, by the authors' scale, they were "light" drinkers. I like to think that I am emulating the scientific father of twins who baptized one and kept the other for a control. I trust that this will not be unkindly construed in the words of Lord Byron as, "What's drinking? A mere pause from thinking!" (To maintain an amino-acid supply, out of respect for my liver, I prescribe a little lean meat now and then.)

HAROLD V. CRANFIELD, M.D.

1074 Sixth Line,
Oakville, Ont.

ABOUT WELFARE STATES AND SEAT BELTS

To the Editor:

As a Canadian resident in the United States, I receive all the American residents' journals. In one of them I came across the following note which I thought so clever that it should be reprinted in one of the Canadian journals, since we are even closer to the brink of a welfare state than they are in the United States.

An anonymous, presumably young, wit of the Cambridge University Medical Society penned the following revision of the most famous Psalm in 1957:

HYMN TO THE WELFARE STATE

The Government is my shepherd,
Therefore I need not work.
It alloweth me to lie down on a good job.
It leadeth me beside still factories;
It destroyeth my initiative.
It leadeth me in the path of a parasite for politics' sake.
Yea, though I walk through the valley of laziness and deficit spending,
I will fear no evil, for the Government is with me.
It prepareth an economic Utopia for me, by appropriating the earnings of my own grandchildren.
It filleth my head with false security;
My inefficiency runneth over.
Surely the Government should care for me all the days of my life!!
And I shall dwell in a fool's paradise forever.

Bulletin of the Los Angeles Medical Society, August 1960.

One other piece of information that appeared in *The A.M.A. News* is that in 1962 all the major automobile manufacturers will include fittings for seat belts in their cars when they leave the factory. This will make it much cheaper and easier for the customer to install seat belts. Also the Chrysler Corporation is supplying their dealers with seat belts at cost for distribution to the customers at cost. The A.M.A. has led the way in convincing the motoring public of the importance of seat belts in preventing the slaughter on the highways, and I feel that we as doctors in Canada should do the same. Many of us have them in our cars, but don't encourage our patients to put them in their cars, as the easiest way possible to help save lives in event of an accident.

K. M. IRWIN, M.D.

Boston Lying-in Hospital,
221 Longwood Ave.,
Boston 15, Mass.

[EDITOR'S NOTE: See McGillivray, J. W., Automobile accidents and seat belts, *Canad. M. A. J.*, 83: 124, 1960, and Peart, A. F. W., in this issue, p. 785.]

REMUNERATION OF DOCTORS BY SALARY

To the Editor:

I have just watched the program "CBC News Magazine" on television (Sunday, March 12, 1961). A new Canadian doctor from Saskatchewan made a statement which all doctors should be prepared to refute. He and others argue about as follows: "Twenty-five to thirty per cent of doctors now *de facto* work for salaries; *ergo*, all doctors could work for salaries".

This is nefarious, insidious and false logic which is foisted on the public by this physician and others who like this line.

1. It is not inherently wrong for a doctor to work on salary. You, Mr. Editor, your staff and the C.M.A. staff do exactly this. This is not obnoxious *per se*.

2. Twenty-five to thirty per cent of doctors in Canada do receive all or mostly all of their incomes from salary. Medical officers of municipal, provincial and federal health and other departments, teachers, medical directors of insurance and pharmaceutical companies, research workers, hospital administrators, etc., are all included in this group.

3. Doctors who render personal health services do not work for salaries. The implication from the aforementioned TV statement is absolutely wrong in this

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regard. Outside of special circumstances, e.g. in outpost areas, in the cottage hospital service in Newfoundland, no doctors render personal health services, as such, on salary. In our C.M.A. questionnaire of last year, 84% of all doctors answering indicated that they would refuse this type of remuneration.

4. Freedom of choice of patient and doctor for personal health services is based on the premise that a physician be remunerated according to the quality of care he is competent to give and to the quality of care medically necessary for the patient's problem. This, sir, is in effect the principle of fee for service.

J. A. MCMILLAN, M.D., C.M.
The Charlottetown Clinic,
200 Queen St.,
Charlottetown, P.E.I.

MEDICAL NEWS IN BRIEF

DIVERTICULUM OF THE FEMALE URETHRA

On the basis of a survey of the literature, Linnet-Jepsen (*Danish M. Bull.* 7: 204, 1960) presents the clinical picture of diverticulum of the female urethra. The diverticula take their origin from the para-urethral ducts. The disease is not at all rare. The symptoms serve as a guide in the diagnosis. The possibility of an urethral diverticulum should be borne in mind in women with recurrent "cystitis", atypical incontinence of urine, anterior vaginal dyspareunia or intermittent vaginal discharge. The diagnosis is often suggested by palpation of the anterior vaginal wall. Urethroscopy should be performed, preferably by means of the McCarthy panendoscope. The most important method of examination is urethrography, which should be performed both as voiding cysto-urethrography and as injection urethrography. These methods may fail and may therefore have to be repeated.

In cases with severe inflammatory infiltration incision should be performed. Extirpation must be advised in chronic symptom-producing cases. However, the frequency of recurrence is relatively high, and there is a risk of postoperative stress incontinence and fistula formation. In order to spare the urethral musculature, careful dissection is necessary, for which reason operation should be postponed until the inflammatory reactions have subsided.

RESPONSE TO IRON IN IRON DEFICIENCY

The utilization of iron given orally was compared with that of iron given parenterally in 12 hospitalized gynecological patients who had severe anemia due to chronic loss of blood. Six received iron-dextran intramuscularly. The other six received ferrous gluconate orally at the rate of 2 g. per day in divided doses. From data on hemoglobin concentration, hematocrit determinations, reticulocyte count and blood volume determinations the rate of utilization was computed.

Pritchard (*J. A. M. A.*, 175: 478, 1961) found that the mean hemoglobin concentration increased 5 g. per 100 ml. in 19 days following parenteral iron and 4.9 g. per 100 ml. in 24 days with oral iron. Since the rate of hemoglobin production averaged 3.0 times normal in the parenterally treated and 2.4 times normal in the orally treated group, there seemed to be little reason for preferring the parenteral route in this situation.

MULTIPLE MYELOMA AND INTRAVENOUS PYELOGRAPHY

The term "myeloma kidney" has been coined to express the pathognomonic significance of depositions of concentric laminated Bence-Jones protein casts in the renal tubules. These may occur in the entire nephron up to the convoluted tubules and result in gradual obstruction. Leucutia (*Am. J. Roentgenol.*, 85: 187, 1961) states that kidney changes have been found in 48 to 90% of reported series of multiple myeloma patients. Renal disease is a common guise under which myeloma may masquerade and elude diagnosis.

Evidence is accumulating which shows that it is hazardous to perform intravenous pyelography in patients with such lesions. In occult cases of myeloma, the use of intravenous pyelography may prove disastrous and result in death from renal failure due to precipitation of intratubular protein.

Intravenous pyelography should not be performed in frank cases of multiple myeloma for any reason. In suspected occult multiple myeloma, electrophoretic studies should be carried out and if protein abnormalities are demonstrated, intravenous pyelography should be omitted. In cases of proteinuria of undetermined cause, the possibility of myeloma should be kept in mind and intravenous pyelography performed only after the elimination of this possibility.

FOLLOW-UP SURVEY OF CLUBFOOT

The results of treatments in a single institution during the past 20 years of 149 patients with clubfoot have been reported by MacEwen *et al.* (*J. A. M. A.*, 175: 427, 1961). This study included patients who were then over five years of age and who returned for clinical and roentgenological evaluation. The 62 patients who returned represented a total of 96 cases of clubfoot. Of the 96 cases, 77 were treated by the Kite plaster method; 19 were treated by manipulations, plaster casts, and Denis Browne splints. Thirty-two operative procedures were performed on the 96 feet.

Excellent or good results were obtained in 72% of the patients treated by plaster casts and the indicated soft tissue surgery. Night splints were found to be important in the prevention and control of recurrences.

(Continued on advertising page 33)

THE LONDON LETTER

COMMONWEALTH MEDICAL ASSOCIATION

This February the British Medical Association has been making one of its increasingly frequent excursions into other lands for its annual meeting. At this meeting in Auckland, New Zealand, one of the more important events was the formation of a Commonwealth Medical Association, a step that has obviously been pending for some time. Previously, the ties between Commonwealth medicine have been kept together loosely at two-year intervals by means of a Commonwealth Medical Conference, such as met in Toronto in 1955, but some countries have felt that there ought to be some provision for better continuity between these meetings. Reluctance to form yet another medical association has in the past been coupled with anxiety as to its financing, but this reluctance was apparently overcome in Auckland, where the latest Commonwealth conference voted unanimously to set up a simple form of secretariat at B.M.A. House, London, with the generous help of the Association's facilities and with Professor D. E. C. Mekie as its honorary executive officer. At the conference which preceded the formation of the new body, which is apparently designed to act only as a clearing house for information between biennial conferences, the Canadian delegate is reported to have voiced Canada's doubts as to the need for a new Association in view of the possible conflict with the World Medical Association, but others were quick to suggest that there need be no conflict of interests. It is not the intention to publish a journal, but to distribute a newsletter to member associations.

TV AND EPILEPSY

The number of clinical syndromes induced by television grows from year to year. Several English writers have recently drawn attention to a condition with which neurologists are becoming familiar but which has not become general knowledge among practitioners. Writing in the *Lancet* of January 28, neurologists from London and Manchester independently describe the induction of epileptic fits by watching television, and later correspondents confirm this finding, which is apparently rare in proportion to the incidence of epilepsy among the general population. One writer draws attention to the fact that in Roman times one of the tests for epilepsy in slaves was to rotate a potter's wheel in front of the subject to induce an attack, since many epileptics respond to an intermittent light stimulus. In the cases described in *Lancet,* attacks were all induced by an attempt to adjust a set which was flickering. When the subject had his face very near to the screen, he lost consciousness and had an attack. In all five cases described, this was the first intimation of a latent epilepsy, and one child had four or five attacks at intervals, each induced by an attempt to adjust a faulty set. It is shown that the flicker stimulus in such cases can be highly specific; for instance, in one case the flicker had to be of frequency 9-30 f.p.s., the source within 35 inches of the patient's eyes, and the eyes preferably shut. The question arises whether the stimulus is reinforced in these cases by an auditory or an emotional stimulus. The suggestion that one sufferer should simply refrain from watching TV was greeted with horror by the parents.

MEDICAL TERMINATION OF PREGNANCY

During February, a member of Parliament sought to introduce a private member's bill widening the legal scope of termination of pregnancy. He wanted to make it legal to terminate pregnancy: (a) for the purpose of preserving the life of the patient; (b) in the belief that there would be grave risk of serious injury to the patient's physical or mental health otherwise; (c) in the belief that there would be grave risk of the child being born grossly deformed or with severe mental or physical abnormality; (d) in the belief that the pregnancy was the result of a criminal offence or that the patient was mentally defective.

As is so common in Britain, the present law on abortion is somewhat haphazard, resting on such judgments as that in the Bourne case when an eminent London gynecologist deliberately aborted a patient pregnant as a result of rape, was tried and acquitted. With this in mind, some English doctors take a liberal view of therapeutic abortion and others are frankly frightened of the legal situation. Moving the second reading of his bill, the sponsor, Mr. Robinson, said that two consequences flowed from this. First was the flourishing trade of the back-street abortionist, and he believed that these gentry performed between 50,000 and 100,000 abortions a year. On the other hand, there were skilled, fully qualified professional abortionists demanding large fees. The House was not, however, impressed with the arguments in favour of the bill, and it was talked out.

SURGEON AND ENGINEER

An annotation in the *Lancet* (Feb. 11) made a plea for co-operation between surgeons and engineers with the establishment of a consulting body manned from both professions. It also started a controversy as to who was to blame for the lack of co-operation in Britain. The writer of the annotation had suggested that the initiative must come from surgeons farsighted enough to appreciate the full resources of present-day mechanical engineering, metallurgy and electronics. One correspondent put the blame on the engineers, who could not at present see the prospect of a first-class career in the field of human engineering. An engineer then retorted that in fact it was the Institution of Mechanical Engineers and not the orthopedists who had organized a symposium on biomechanics in 1959, that engineers interested in biomechanics were not rare but that the surgeon tended only to want answers to his day-to-day problems, to the neglect of long-term research. Others then pointed to the recent formation of a Biological Engineering Society in Britain, providing opportunity for exchange of ideas between its members, who may be engineers, physicists, biologists or surgeons. It is further suggested that a central research institute of biomechanics should be set up in the United Kingdom.

S. S. B. GILDER

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ASSOCIATION NOTES

THE MEDICO-LAY AFFILIATES OF THE CANADIAN MEDICAL ASSOCIATION

NATIONAL HEART FOUNDATION OF CANADA

JOHN B. ARMSTRONG, M.D., F.R.C.P.[C]
Executive Director

[This is the fourth of a series of articles describing the organization and work of the voluntary health agencies and other medico-lay bodies affiliated with the Canadian Medical Association.]

OBJECTS

THE NATIONAL Heart Foundation of Canada was founded "to co-ordinate and correlate the efforts of organizations and individuals interested in heart diseases, with a view to reducing the morbidity and mortality therefrom in Canada".

It was formed as a federation of the Provincial Heart Foundations, other organizations and persons devoted to the study and prevention of heart and blood vessel disease by the support of research, and the dissemination of knowledge through professional and public education.

HISTORY

The National Heart Foundation was incorporated under Part II of the Companies Act on June 1, 1596. It arose from a National Conference on Heart Disease, held on January 16, 1956, in Ottawa, under the authority of the Minister of National Health and Welfare and sponsored by that body of doctors especially interested in diseases of the heart, the Canadian Heart Association. It is the only national voluntary agency in Canada that directs its activities solely to the cardiovascular field, and to the control of cardiovascular disease.

The National Heart Foundation received generous support in its formative stages, from the Heart Association and the Canadian Life Insurance Officers Association. To raise funds for research and education in heart disease, it was necessary to launch an Annual Heart Fund Campaign. One such appeal has been held throughout Canada each year in the month of February. The first Canadian Heart Fund in 1958 realized $600,000; the latest in 1960 increased to almost one million dollars.

ORGANIZATION

There are six Provincial Heart Foundations, from Quebec to British Columbia, federated in the National Heart Foundation. In addition there is an Atlantic Provinces Division of the National Foundation. In each province, there are chapters, committees, or other local organizations that carry forward the work of the Heart Foundations.

CURRENT ACTIVITIES

RESEARCH: The primary responsibility of the Heart Foundations is the support of research in the cardiovascular field. To assure the best possible use of the money entrusted to them by the public of Canada, the Heart Foundations have set up a system of application and review by acknowledged medical experts that is the equal of any such system in the country. There are two levels of careful scrutiny and assessment before submission to the governing Board for final approval.

The research program undertakes the support of people devoted to research by a Fellowship Program, and the support of projects by a Grant-in-Aid Program. The Fellowship program helps Canada to gain and retain top scientists in this field. In project research, the Foundations underwrite the cost of approved assistants and equipment, but, contrary to common belief, do not pay the principal investigator to carry out the research.

EDUCATION: As more information about the control of heart disease becomes available, the Heart Foundations feel obliged to pass this information on to those who can make the best use of it.

Technical information is directed to the medical and ancillary groups by a program of professional education. Non-technical information is directed to the public through the mass media and to selected groups by more direct contact. It is felt that much that is of help to the heart patient and his relatives could be made available to him through his doctor's office.

The Heart Foundations do not participate in patient-care programs, and do not have a service program in the usual sense.

FINANCE:

Budget 1959—$1,101,124.00	*Reserve Funds**
REVENUE:	
Heart Fund Campaign	$666,052.00
Community Chest, United Appeal, etc.	40,000.00
Grants—Federal	nil
Provincial	156,000.00
Municipal	nil
Other	35,913.00
Membership fees	227.00
Reimbursement for services rendered	nil
Revenue from publications	nil
Bequests	5,202.11
Other (memorial and miscellaneous gifts)	76,616.39
	$980,010.50
Campaign expense expressed as percentage of total revenue	9.4%
EXPENDITURE:	
Education	$ 54,000.00
Research	495,000.00
Service	nil
Administration	128,000.00
Campaign	93,000.00
	$770,000.00

*Reserve funds June 30, 1959	$451,705.00
Research Commitments—July 1, 1959—June 30, 1960	457,397.00
Deficit—Commitments over Reserve	5,692.00

MEDICAL REPRESENTATION

The Board of Directors of the National Heart Foundation and of each of its affiliated Provincial Foundations have medical advisory committees that consider all matters of a medical nature. In addition, all of the Foundations have prominent doctors as members of their Boards.

THE HEALTH PROBLEM

The cardiovascular diseases have become Canada's primary health problem. They account for almost half of the deaths in this country each year. They are the most common form of chronic disability. It has been reliably estimated that one and a quarter million Canadians have some form of heart or blood vessel disease. These patients represent eighty million dollars lost annually in salaries and wages, and another one hundred and twenty million dollars annually as a loss of productive capacity in the care thereof.

Knowledge in the cardiovascular field has progressed further in the past fifteen years than in the previous fifteen centuries. One has only to reflect on the advanced techniques employed in the diagnosis and surgical management of a congenital heart problem to realize the fruits of the progress that is being made. The future looks bright for the ultimate control of atherosclerosis, the cause of over 80% of cardiovascular problems.

Much can be done for the "coronary" or "stroke" patient today. Just as the late President Roosevelt did so much for poliomyelitis, so President Eisenhower has shown dramatically that these patients can, and should, return to work. It is now known that over 85% of patients can return to their original job after their first myocardial infarction, and that 45% of patients after their first cerebral thrombosis can care for themselves, the majority returning to work.

The National Heart Foundation of Canada and all its affiliated provincial groups will continue to devote all their efforts to the control and prevention of cardiovascular disease through research and education. In these efforts they are gaining the confidence of an ever-increasing number of Canadians in all walks of life.

The offices of the Foundation are at 501 Yonge Street, Toronto 5.

THE NINETY-FOURTH ANNUAL MEETING

VENEZ A MONTREAL EN JUIN!

LE PROGRAMME SCIENTIFIQUE

Les comités du programme, aussi bien celui de Montréal que celui de Toronto, se sont efforcés cette année de préparer un plan destiné à faire connaître au médecin praticien les nouvelles disciplines de diagnostic et de traitement. Ces séances éducatives commenceront le mardi matin 20 juin et se continueront pendant les trois autres jours. Comme elles constituent en somme des cours de perfectionnement, elles comprendront des discussions sur la médecine, la chirurgie, la pédiatrie, l'anesthésie, l'obstétrique et la gynécologie.

Des conférenciers spéciaux parleront, le mercredi et le jeudi, de médecine, d'anesthésie et de psychiatrie. Jeudi matin, un grand chirurgien de Suède, le professeur Hugo Rosenqvist, chef du service de chirurgie de l'hôpital du Sud, à Stockholm, prononcera un éloge à Lister. Parmi les autres invités de marque, mentionnons le Dr Charles M. Fisher, du service de neurologie du Massachusetts General Hospital, de Boston; le Dr LeRoy D. Vandam, du service d'anesthésiologie du Peter Bent Brigham Hospital, aussi de Boston et le Dr D. Ewen Cameron, de l'Allan Memorial Institute, de Montréal. Les médecins de langue française auront le plaisir d'entendre un obstétricien français réputé, le professeur Maurice Mayer, chef du service d'obstétrique à l'hôpital Saint-Antoine de Paris.

La journée du vendredi, 23 juin, a été réservée aux questions d'économie médicale. Il y aura conférences et forum sur l'assurance pour soins médicaux et sur plusieurs autres sujets connexes. Au cours de la matinée, les congressistes pourront écouter l'hon. Emmet M. Hall, juge en chef de Saskatchewan, qui vient d'être nommé président de la Commission royale chargée par le gouvernement Diefenbaker de faire enquête sur les services médicaux du pays, qui parlera du rôle de cet organisme. Le Dr T. J. Quintin, de Sherbrooke, de retour d'un voyage aux antipodes, parlera de l' "Assurance-santé en Australie" tandis que le Dr Hugo Rosenqvist relatera ce qui se passe en Suède à ce sujet.

Un médecin de Saskatoon, le Dr H. D. Dalgleish, expliquera à ses auditeurs ce qui s'est passé en Saskatchewan dans le domaine de l'assurance-santé depuis, quelques mois et de l'expérience acquise par les membres de la profession. D'autres conférenciers traiteront des relations qui existent entre les médecins et les gouvernements.

Un autre aspect intéressant du programme scientifique sera la présentation de plusieurs films inédits sur des sujets d'actualité médicale.

LE PROGRAMME MONDAIN

Les membres de la Division du Québec seront nécessairement les hôtes de leurs confrères des autres provinces au cours de ces assises médicales nationales. Le programme qu'ils ont préparé avec soin promet d'être fort apprécié des participants. Ainsi le lundi 19 juin, les médecins et leurs épouses seront conviés à une dégustation de vins, agrémentée de charcuteries, de fromages et de pâtisserie. Cette dégustation aura lieu au musée des Beaux-Arts, rue Sherbrooke et plus de quinze vins délicieux seront servis.

Le grand dîner annuel au Conseil général aura lieu dans la salle de bal de l'hôtel Reine Elizabeth le mardi soir et les organisateurs locaux promettent aux assistants des divertissements de haut ton. Tout le monde est invité.

L'assemblée générale annuelle de la Division du Québec aura lieu le mercredi midi. Un repas léger sera servi et nos amis de la province de Québec se mettront à l'œuvre immédiatement après pour entendre le rapport des activités de la division et ensuite pour élire les membres de leur exécutif pour la prochaine année.

Le soir du même jour, assemblée annuelle de l'association nationale. La cérémonie commencera à 8 h.

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15 de la soirée. Il y aura d'abord installation du nouveau président, puis la nomination du major-général Georges-P. Vanier, D.S.O., M.C., C.D., gouverneur-général du Canada comme membre à vie de l'association. Fait intéressant à noter, le général Vanier sera le troisième profane à recevoir cet honneur. Les deux autres sont aussi d'éminents personnages: le très honorable Vincent Massey, ancien gouverneur-général du Canada et Son altesse royale le duc d'Edimbourg.

La séance se terminera par la nominatin des membres seniors désignés par les Divisions.

On pourra lire dans une édition subséquente du Journal, les détails du programme des activités féminines.

BIENVENUE À MONTREAL

Peu de médecins de langue française ne connaissent pas la ville de Montréal, métropole de notre pays. L'ancien village indien d'Hochelaga, devenu Ville-Marie le 18 mai 1642 grâce à la prévoyance de Paul de Chomedy, Sieur de Maisonneuve, est aujourd'hui une des plus grandes villes du monde. Incorporée en 1832, la cité de Montréal a été longtemps, après l'union du Haut et du Bas Canada, en 1841, le siège du gouvernement du pays. Sa population est maintenant de 1,700,000 habitants et son caractère bi-ethnique en fait un des centres touristiques les plus connus d'Amérique.

Point n'est besoin d'insister sur le choix des endroits à visiter. Le vieux Montréal, près du port, conserve encore tous ses charmes. Puis il a l'Oratoire St-Joseph, où plus de trois millions de pélerins se rendent chaque année, le Château de Ramezay, le Jardin Botanique, l'Observatoire du Mont-Royal, le musée des Beaux-Arts et combien d'autres choses à voir.

Pour ceux qui veulent se récréer le soir, les clubs de nuit sont nombreux et leur cuisine, comme leurs spectacles, est réputée. Il n'y a que l'embarras du choix. D'autres détails sur Montréal un peu plus tard.

MEDICAL MEETINGS

THE MONTREAL PHYSIOLOGICAL SOCIETY

The Montreal Physiological Society held its second regular meeting for the 1960-1961 season at the plant of the Ciba Company, Dorval, on March 8. Dr. Carl Schaffenberg welcomed the members of the Society and guests and pointed out that this was the first scientific meeting to be held in the auditorium of Ciba's new building.

The meeting commenced with a special lecture. Dr. J. Sanford Hart of the Division of Applied Biology, National Research Council, Ottawa, spoke on "Acclimatization of Native Peoples". Dr. Hart illustrated his talk with a film. This showed glimpses of investigations carried out at Pangnirtung in the Eastern Arctic studying Eskimos and using the scientists of the expedition as control subjects. Scenes were also shown illustrating work that has been conducted with the Crow Indians of the Yukon and the Indians of Tierra del Fuego in South America. Episodes in an Australian project studying the ability of the aborigines to sleep naked in the cold were also shown. Dr. Hart discussed these studies, particularly those involving the work with Eskimos. There is a suggestion that these individuals produce more heat than control subjects. They were better able to sleep in the cold, and their foot skin temperature did not drop as much as did that of the controls. Dr. Hart stressed, however, the technological achievements of the Eskimos, who have devised superb clothing and shelter in order to live in the inhospitable environment of the Canadian Arctic. This factor would appear to be even more significant in explaining their survival than any physiological acclimatization.

After a buffet supper a business session was held and three new members were elected: Dr. W. G. Krauser, Dr. S. P. Bhatnagar and Dr. N. K. M. de Leeuw. This was followed by the scientific session chaired by Dr. A. S. V. Burgen, at which the following papers were presented: "The Identification of the Porter-Silber Chromogen Secreted by the Rat Adrenal" —Pamela Ward and Marion K. Birmingham; "Effect of Nialamide on Plasma and Adrenocorticosterone in Rats"—G. Jasmin and C. Lise Richer; "Effects of Enzyme Inhibitors on the Maintenance of Auricular Arrhythmias"—P. G. Roy; "Pathological Lesions Produced in Rats by Repeated Injection of Gums"—A. Hajdu and J. D. McColl; "Quantitative Interaction Between Dextran and Antihistamines in the Rat"—L. Kate and B. Gozsy; "Effect of Amygdaloid Lesions on Plasma Corticosterone Response of the Albino Rat to Emotional Stress: A Preliminary Study"—E. W. Bovard and P. Gloor; "Some Pharmacological Effects of Parachlorophenylethylamine"—J. M. Parker, Norah Hildebrand and B. K. Wasson; "Further Studies on the Cardiovascular Actions of Antisympathomimetic Drugs" —B. G. Benfey and D. R. Varma.

J. M. PARKER

THIRD WORLD CONGRESS OF PSYCHIATRY

An outstanding feature of the Third World Congress of Psychiatry, to be held in Montreal from June 4 to 10, 1961, will be a session on Scientific Creativity. This will include discussions by three Nobel Prize winners: Lord Adrian, Master of Trinity College, Cambridge, and Vice-Chancellor of Cambridge University; Dr. Szent-Gyorgyi, of the Research Institute of Muscle Research at Woods Hole, Massachusetts; and Dr. Linus Pauling, Professor of Chemistry at the California Institute of Technology.

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

1960 CERTIFICATION EXAMINATIONS

The candidates whose names are listed below were successful in the 1960 Certification examinations in the specialties of Therapeutic Radiology, General Surgery, Neurosurgery, Obstetrics, Obstetrics and Gynecology, Ophthalmology, Orthopedic Surgery, Otolaryngology, Plastic Surgery, Thoracic Surgery, and Urology. (See also p. 448, issue of February 25, and p. 506, issue of March 4.)

SPECIALTY OF THERAPEUTIC RADIOLOGY (14)

BERNIER, RAYMOND M.D.(Laval) 1955	Hôpital St-Michel, Roberval, Que.
BLACKBURN, ROBERT M.D.(Laval) 1953	1385, rue Portland, Sherbrooke, Que.
BOCIEK, ROBERT CARL M.D.(Ottawa) 1955	17 Labelle Avenue, Sault Ste. Marie, Ont.
BREWIN, THURSTAN BERKELEY M.B., B.S.(London) 1949	163 Dromore Crescent, Hamilton, Ont.
BROWN, BASIL ST. JOHN M.B., B.S.(London) 1951	Department of Medicine, Queen Mary Veterans Hospital, Montreal 26, Que.
DESLAURIERS, GABRIEL M.D.(Montreal) 1950	790 St-Louis, Ville St-Joseph, St-Hyacinthe, Que.
HELLMUTH, FRITZ-HEINZ KARL W. M.D.(Christian-Albrechts University, Kiel) 1953	Radiotherapy Department, Winnipeg General Hospital, Winnipeg 3, Man.
HOOPER, WILLIAM TEMPLE M.D., C.M.(McGill) 1945	Division of Cancer Control, Health Centre, 188 Prince Street, Charlottetown, P.E.I.
MEIKLE, ALEXANDER LIDGATE, M.B., Ch.B.(Edinburgh) 1942	Department of Radiotherapy, St. Boniface Hospital, St. Boniface, Man.
MERRIAM, RICHARD KERR M.D., C.M.(Dalhousie) 1952	Drawer 608, Red Deer, Alta.
MOK, GEORGE CHI-KWONG M.D.(Lingnan University, Canton, China) 1951	The Ontario Cancer Foundation, Windsor Clinic, Metro. General Hospital, Windsor, Ont.
MUIRHEAD, WILLIAM M.B., Ch.B.(Edinburgh) 1951	23 West 33rd Street, Hamilton, Ont.
NICHOL, JAMES THOMPSON M.D.(Western Ontario) 1953	198 Macy Boulevard, Apt. 206, Ottawa 3, Ont.
WHITTINGHAM, DAVID SPENCER M.D.(Toronto) 1950	198 Macy Boulevard, Apt. 108, Ottawa 3, Ont.

SPECIALTY OF GENERAL SURGERY (71)

ABBOTT, CLIFFORD EDWARD BULMAN M.D.(Manitoba) 1955	4053 Warrensville Center Rd., Apt. 21, Cleveland 22, Ohio, U.S.A.
BARSKY, MORLEY M.D.(Manitoba) 1956	138 Machray Avenue, Winnipeg, Man.
BEAUDOIN, GHISLAIN M.D.(Laval) 1952	626 Iberville, Jonquière, Que.
BERGERON, Claude M.D.(Laval) 1956	2767, rue Maplewood, Apt. 410, Montreal 26, Que.
BETTER, NED M.D.(Geneva) 1954	2535 Nantel Street, Ville St-Laurent, Que.
BOURGEOIS, DIDACE CHARLES M.D.(Laval) 1956	Hôtel-Dieu St.Vallier, Chicoutimi, Que.
BRANDL, THOMAS M.R.C.S.(Eng.), L.R.C.P.(Lond.) 1946	40 Coldwater Street East, Orillia, Ont.
BROOKS, VIVIAN EARL HAMILTON M.D., C.M.(McGill) 1954	c/o Dr. S. E. Brooks, 6A Westminster Crescent, Half-Way-Tree P.O., Jamaica, B.W.I.
BUIE, WILLIAM JOHN M.D.(Alberta) 1954	2940 - 17 Avenue S.W., Calgary, Alta.
BUREAU, JULES M.D.(Montreal) 1956	344, 1ère avenue sud, Sherbrooke, Que.
BUTT, ROBERT MURCELL M.D., C.M.(McGill) 1954	5425 Bessborough Avenue, Montreal, Que.
DEEGAN, FRANCIS KENNETH M.D.(Ottawa) 1955	124 Beckwith Street, Smiths Falls, Ont.
DESHAIES, BENOIT ARISTIDE M.D.(Montreal) 1955	11375 rue Meunier, Montreal 12, Que.
DESJARDINS, JEAN GAUTHIER M.D.(Montreal) 1956	3445 avenue Papineau, Apt. 3, Montreal, Que.
DION, RAYMOND-MARIE M.D.(Laval) 1952	24 rue St-Dominique, Hull, Que.
DOVER, MARK ROBERT M.D.(Ottawa) 1955	150 Metcalfe Street, Ottawa 4, Ont.
DOWNS, ALLAN RAE M.D.(Manitoba) 1954	790 Sherbrook Street, Winnipeg 2, Man.
ELLIOTT, ROBERT CHARLES M.D., C.M.(Queen's) 1944	Toronto Military Hospital, Sunnybrook P.O., Toronto 12, Ont.
FALLIS, JAMES CORYELL M.D.(Toronto) 1955	211 College Street, Apt. 142, Toronto, Ont.
FRIEDMAN, MORRIS HAROLD W. M.D.(Alberta) 1954	11219 - 100 Avenue, Edmonton, Alta.
GAZLEY, LORNE ALBERT M.D.(Toronto) 1952	No. 3, Fighter Wing H.Q., C A P O 5055 Canadian Armed Forces, Europe.
GOODING, JOHN THEODORE M.D., C.M.(McGill) 1954	6 Burton Road, Forest Hill, Toronto, Ont.
GOSSELIN, CAMILLE M.D.(Laval) 1956	268, rue Saunders, Quebec 6, Que.
GOUWS, FRANS BAREND CHRISTOFFEL L.R.C.P., L.R.C.S.(Edinburgh) 1951	The Parsons Clinic, Box 608, Red Deer, Alta.
GROVES, KENNETH PRYDE M.D.(Toronto) 1932	1404 Medical-Dental Bldg., 925 West Georgia Street, Vancouver, B.C.
HORSLEY, JAMES IRWIN M.D.(Medical Evangelists, California) 1945	50 Sheppard Avenue East, Willowdale, Ont.
INGLIS, FREDERIC GRAHAM M.D., C.M.(Dalhousie) 1955	5546 Gatineau Avenue, Montreal, Que.
JOHNSTON, FRANK DORRENS M.B., Ch.B.(Edinburgh) 1950	Grace Hospital, 200 Arlington Street Winnipeg, Man.
KERR, JAMES IAN M.D.(Toronto) 1955	253 The Donway West, Apt. 6, Don Mills, Ont.
KWAK, JOHN M.D.(Toronto) 1955	229 Olive Avenue, Oshawa, Ont.
LECLERC, JEAN-LOUIS M.D.(Laval) 1955	2071 Chemin Ste-Foy, Quebec 10, Que.
LEE, ROBERT EDMUND MUSGRAVE M.D.(Manitoba) 1952	Box 10, Terrace, B.C.
LEJEUNE, LOUIS-PHILIPPE M.D.(Montreal) 1955	2360, rue Verdun, Sherbrooke, Que.
LINTON, HAROLD M.D.(Toronto) 1939	744 Oak Street, Winnipeg, Man.

LITTLE, ROBERT DAVIDSON M.B., Ch.B.(Aberdeen) 1953	Kickham Clinic, Westlock, Alta.
MACDONALD, JOHN ALEXANDER M.D.(Toronto) 1953	6 Rosemarie Drive, Scarborough, Ont.
MARTIN, JAMES WALTER M.D.(Western Ontario) 1954	332 Guelph Line, Apt. 7, Burlington, Ont.
McKINNON, FRANCIS ALEXANDER M.D., C.M.(Queen's) 1952	11 Ballymena Court, Don Mills, Ont.
MILLS, DOUGLAS GEORGE M.D.(Toronto) 1955	743 Simcoe Street North, Oshawa, Ont.
MITCHELL, ROBERT IAN M.B., B.S.(Sydney Univ.) 1951	82 Forest Grove Drive, Willowdale, Ont.
MOFFAT, WILLIAM WRIGHT M.D., C.M.(McGill) 1953	18 Barbara Crescent, Toronto, Ont.
MORGAN, BRUCE EVAN M.D., C.M.(Queen's) 1951	Fort Churchill Military Hospital, Fort Churchill, Man.
NEWTON, WILLIAM EVANS M.D., C.M.(McGill) 1951	410 - 4th Floor, Medical Arts Building, Victoria, B.C.
PAILLE, JOSEPH BERNARD JEAN GUY M.D.(Laval) 1956	308 Celanese, Drummondville, Que.
PALMER, MARVEN FRASER M.D., C.M.(McGill) 1954	3 Hermitage Court, Fredericton, N.B.
PARSONS, FRANK WATSON M.D., C.M.(McGill) 1952	The Wainwright Clinic, Wainwright, Alta.
PATRY, PAUL-EMILE M.D.(Laval) 1954	618, rue Fraser, Quebec, Que.
PISESKY, WALTER M.D.(Alberta) 1955	13943 - 107 A. Avenue, Edmonton, Alta.
POLLOCK, ALEXANDER M.D., C.M.(Queen's) 1954	523 Garrison Crescent, Saskatoon, Sask.
POOLE, NORMAN LESLIE M.D., C.M.(McGill) 1954	The Montreal General Hosp., 1650 Cedar Avenue, Montreal 25, Que.
QUINN, MICHAEL HUGH FRANCIS M.D.(Ottawa) 1955	211 King Street, St. Catharines, Ont.
RAILTON, RICHARD HAZLEWOOD M.D.(Toronto) 1955	335 St. Clair Avenue East, Toronto 7, Ont.
RAZA, LORNE NOEL M.D.(Geneva, Switzerland) 1954	8 Kings Point Drive, Apt. 10, Toronto 18, Ont.
REID, IAN LIVINGSTONE M.D.(Manitoba) 1956	353 Eveline Street, Selkirk, Man.
SAINT-LAURENT, ROMULUS M.D.(Laval) 1951	3360 Chemin Côte Ste-Catherine, Apt. 9, Montreal 26, Que.
SALES, JACK LEROY M.D.(Western Ontario) 1955	50 Walmer Road, Apt. 108, Toronto 4, Ont.
SALGADO, ISIDRO M.D.(Madrid Medical School) 1951	4970 Queen Mary Road, Montreal, Que.
SHELTON, PETER JAMES M.D.(Manitoba) 1950	773 Selkirk Avenue, Winnipeg 4, Man.
SINCLAIR, JOHN NORMAN M.D.(Ottawa) 1953	11 Coldwater, Orillia, Ont.
SPROULE, WILLIAM GLENN M.D.(Ottawa) 1955	34 Farm Street, Almonte, Ont.
STRAUSS, GERALD Z. M.D.(Toronto) 1955	106 Lyndock Crescent, Don Mills, Ont.
SUDERMANN, Peter M.D.(Göttingen, Germany) 1950	Estevan Clinic, 1323—4th Street, Estevan, Sask.
THEOCHARIDES, PETER M.D.(Paris) 1956	5045, boulevard Lasalle, Montreal 19, Que.
THOMSEN, ANDREAS EINAR THINGBERG M.D.(Amsterdam) 1950	Charles Camsell Hospital, Edmonton, Alta.
TREMBLAY, RENÉ-GEORGES M.D.(Laval) 1956	605—111ième rue, Shawinigan, Co. St-Maurice, Que.
ULRICH, DONALD GEORGE M.D.(Alberta) 1946	128—624 Sixth Street, New Westminster, B.C.
UPMALIS, ILGVARS HENRY M.D.(Western Ontario) 1955	97 Frederick St., Kitchener, Ont.
VALLEE, JEAN-GUY M.D.(Laval) 1955	5401 Brodeur, Notre-Dame de Grace, Montreal, Que.
VIGNEAULT, MOISE M.D.(Laval) 1943	5100 boulevard Pie IX, Apt. 302, Montreal, Que.
WATSON, ROBERT JAMES M.D.(Toronto) 1954	27 Elgin St., Lindsay, Ont.
WILLIAMS, HOWE BRUCE M.D., C.M.(McGill) 1955	5574 Decelles Ave., Apt. 2, Montreal 26, Que.

SPECIALTY OF NEUROSURGERY (4)

BERGER, EMILE M.D.(Austria) 1951	4888, avenue Grosvenor, Montreal, Que.
IVAN, LESLIE PAUL M.D.(Debrecen, Hungary) 1944	Medical Arts Clinic, Regina, Sask.
POSNIKOFF, JACK M.D.(Toronto) 1952	1125 East 17th St., Suite 114, Santa Ana, Calif., U.S.A.
SCHACTER, IRVING BERNARD M.D.(Toronto) 1949	99 Avenue Road, Toronto 5, Ont.

SPECIALTY OF OBSTETRICS (1)

AMYOT, GILLES M.D.(Montreal) 1956	6895—44 avenue, Rosemount, Montreal 36, Que.

SPECIALTY OF OBSTETRICS AND GYNECOLOGY (41)

BECK, ROLAND PETER M.D., C.M.(Queen's) 1955	562 Albert St., Kingston, Ont.
BERNIER, ANDRÉ HUBERT M.D.(Laval) 1955	Bic, Rimouski, Que.
BERTRAND, NORRIS RALPH M.D.(Alberta) 1948	3244 Alfege Street, Calgary, Alta.
BIRCHARD, JAMES RUSSELL M.D., C.M.(Queen's) 1954	179 Berry Road, Apt. 103, Toronto, Ont.
BROWN, ELDON JAMES M.D.(Western Ontario) 1955	438 Burdick Street, London, Ont.
BURNETT, ALEXANDER MACGOWAN M.D.(Western Ontario) 1954	288 Park Street, Peterborough, Ont.
CROOKS, HUGH JAMES M.D.(Alberta) 1954	11121—85th Avenue, Edmonton, Alta.
DAVIES, MATTHEW M.D.(Alberta) 1943	9—1st Street S.W., Medicine Hat, Alta.
DORAN, TERENCE ALEXANDER M.D.(Toronto) 1953	234 Kingsdale Avenue, Willowdale, Ont.
DUNNETT, IAN PROCTER M.B., Ch.B.(Edin.) 1949	Dept. of Obstetrics and Gynecology, Vancouver General Hospital, Vancouver 9, B.C.
FISH, EDWARD JAMES LAURENCE M.D.(Alberta) 1954	201—33 Avenue S.W., Calgary, Alta.
FREIER, ANDREW AMMUD M.B., B.S.(London) 1947	1579 Ouellette Avenue, Windsor, Ont.
HANNAH, WALTER JONES M.D.(Western Ontario) 1953	8 Redwing Place, Don Mills, Ont.

HARASZTHY, DENNIS VINCENT M.D.(Pazmany Peter Univ., Budapest, Hungary) 1948	394 Bloor Street West, Toronto, Ont.
IRWIN, NOBLE TOTTON M.D.(Manitoba) 1950	Toronto General Hospital, Toronto, Ont.
JUBB, EDITH DAWNE M.D.(Toronto) 1951	244 Bloor Street West, Toronto 5, Ont.
KOSASKY, HAROLD JACK M.D.(Manitoba) 1953	c/o B. Johnston, Brewer's Mills, Ont.
LAFRENIERE, JEAN M.D.(Laval) 1954	1185, rue Hart, Trois-Rivières, Que.
LAROCHELLE, RÉMI JEAN M.D.(Laval) 1954	5521 est, Bélanger, Montreal, Que.
LEMAY, JEAN M.D.(Laval) 1953	139 Wanda, Apt. 3, Eastview, Ottawa 2, Ont.
MACKAY, JOHN ERNEST M.D., C.M.(McGill) 1954	134 Diamond Hill Road, Warwick, Rhode Island, U.S.A.
MOORE, DONALD CHARLES M.D., C.M.(Dalhousie) 1953	121 Southill Drive, Don Mills, Ont.
MURPHY, JOHN KEVIN M.B., B.Ch., B.A.O. (Trinity College, Dublin) 1954	108 Medical and Dental Building, Regina, Sask.
MURRAY, DONALD JAMES M.D.(Alberta) 1954	The Smith Clinic, 4815—51st Street, Camrose, Alta.
OSTIGUY, GÉRARD GUY M.D.(Montreal) 1954	5033—16e avenue, Rosemount, Montreal 36, Que.
PLATT, MELVILLE ALBERT M.D.(Western Ontario) 1952	360 Queen's Avenue, London, Ont.
RAYNES, MARVIN M.D.(Manitoba) 1956	616 Medical Centre, Apt. 3, Winnipeg 3, Man.
RINGROSE, CHARLES ALEXANDER DOUGLAS M.D.(Alberta) 1954	11140—68th Avenue, Edmonton, Alta.
RUSSELL, EDGAR ALEXANDER M.D.(Manitoba) 1946	2134 Ewart Avenue, Saskatoon, Sask.
RYAN, SAMUEL FRANCIS M.B., B.Ch., B.A.O. (Trinity College, Dublin) 1954	1303 York Avenue, New York 21, N.Y., U.S.A.
SCHULZE, WERNER BERNHARD M.D.(Marburg, Germany) 1954	11233—96th Street, Edmonton, Alta.
SKAIN, FRANK JOSEPH M.D.(Toronto) 1954	33 Bannockburn Avenue, Toronto, Ont.
STAPLEFORD, EDMUND MCCULLOCH M.D.(Western Ontario) 1953	137 Wellington Street, Sarnia, Ont.
TAYLOR, CLIFFORD RAYMOND M.D.(Toronto) 1955	1435 Alfred Crescent, Burlington, Ont.
TOREM, MARTIN M.D.(Toronto) 1954	833 Bayview Avenue, Apt. 204, Leaside, Toronto 17, Ont.
TRUDEL, ANDRÉ M.D.(Laval) 1954	80 rue Brooks sud, Sherbrooke, Que.
TURMEL, JEAN M.D.(Laval) 1955	31 rue Guénette, Lévis, Que.
VAN PRAAGH, IAN GERALD LOU M.D.(Toronto) 1955	332 Sheldrake Boulevard, Toronto 12, Ont.
WEBB, DONALD ARTHUR M.D.(Alberta) 1951	1940 Lonsdale Avenue, North Vancouver, B.C.
WILSON, RICHARD M.D.(Toronto) 1954	31 Alexander Street, Apt. 317, Toronto 5, Ont.
WOOD, ANGUS ELDON M.D.(Manitoba) 1956	821 Jackson Crescent, New Westminster, B.C.

SPECIALTY OF OPHTHALMOLOGY (16)

ANHALT, EDWARD FREDERICK M.D.(Manitoba) 1956	713 Columbia Street, New Westminster, B.C.
BRADLEY, BRIAN MICHAEL M.D.(Western Ontario) 1954	270 Christina Street North, Sarnia, Ont.
COLLYER, ROBERT TALBOT M.D.(Western Ontario) 1955	7 Chalmers Street, London, Ont.
COULDWELL, WILLIAM JOHN M.D., C.M.(McGill) 1950	403 Sixth Street, Suite 210, New Westminster, B.C.
EDWARDS, GEORGE KEITH M.D.(Western Ontario) 1954	Medical Arts Building, Suite G-5, 180 Metcalfe St., Ottawa, Ont.
HEROLD, WALTER EDMUND M.D.(Leipzig) 1931	98 Pembroke Street West, Pembroke, Ont.
KUSHNER, ARNOLD GRAHAM M.D., C.M.(McGill) 1954	832 Decarie Boulevard, Montreal 9, Que.
MCCREERY, ROBIN GORDON M.D.(Western Ontario) 1954	5780 Cambie St., Suite 130, Vancouver 15, B.C.
MCGILLIVRAY, DUNCAN WRAY M.D.(Western Ontario) 1954	769 Paling Road, Burlington, Ont.
MCKENZIE, THOMAS ROBERT M.D.(Western Ontario) 1954	1542 Bruce Avenue, Windsor, Ont.
MORTIMER, CLIVE BENNETT M.B., B.Chir.(Cambridge) 1954	28 Cecil Street, Toronto 2B, Ont.
ROSENBAUM, PETER M.D., C.M.(McGill) 1954	3777 Côte des Neiges, Apt. 424, Montreal, Que.
STEAD, STANLEY M.B., Ch.B.(Manchester) 1951	602 Medical-Dental Bulding, Regina, Sask.
TANNER, WILLIAM HAROLD REGINALD M.D.(British Columbia) 1954	278 Glengrove Avenue West, Toronto 12, Ont.
TURNBULL, JOHN BERTRAM M.D.(Manitoba) 1954	Medical Arts Clinic, 2125 - 11th Avenue, Regina, Sask.
VAILE, SIGMUND JEROME M.D.(Toronto) 1955	416 Glengrove Avenue West, Toronto 12, Ont.

SPECIALTY OF ORTHOPEDIC SURGERY (21)

ALMS, MICHAEL M.B., Ch.B.(Bristol) 1945	314 MacMillan Building, Saskatoon, Sask.
BARTLETT, LESLIE HAMER M.D., C.M.(McGill) 1952	6657 Laburnam Street, Vancouver, B.C.
BLAIR, EDWARD JAMES M.D.(Western Ontario) 1954	193 Ontario Street, St. Catharines, Ont.
COWAN, JOHN DAVID EARLE M.D., C.M.(Dalhousie) 1951	33 Monkstown Road, St. John's, Nfld.
DALE, GEORGE GORDON M.D.(Toronto) 1954	24 Tarlton Road, Toronto, Ont.
DESJARDINS, DENIS R. M.D.(Ottawa) 1955	247 Emond Street, Ottawa 2, Ont.
EDWARDS, GLEN ELMER M.D.(Alberta) 1954	4012 Glenpark Cres., Suite 3, Calgary, Alta.
FERLAND, JEAN-JACQUES M.D.(Laval) 1955	725 Champfleury, Quebec 3, Que.
GREENWOOD, FREDERICK ALAN HAMILTON M.D., C.M.(McGill) 1954	50 Roxton Crescent, Montreal West, Que.
GROGONO, BASIL JOHN STEELE M.B., B.S.(London) 1945	989 Dorchester, Winnipeg, Man.
HUDECKI, STANLEY MICHAEL M.D.(Toronto) 1940	Medical Arts Building, 1 Young Street, Hamilton, Ont.
LEMAIRE, RAYMOND M.D.(Laval) 1956	27 Terrasse Paquin, Pont Viau, Que.

LOTTO, WALLACE NEIL M.D.(Toronto) 1947	Professional Suites, Toronto Western Hospital, 399 Bathurst Street, Toronto, Ont.
PAPINEAU, LOUIS-JOSEPH M.D.(Montreal) 1952	2921 Quévillon, Montreal 36, Que.
PORRITT, PETER NORMAN M.R.C.S.(Eng.), L.R.C.P.(Lond.) 1946	Manitoba Clinic, 790 Sherbrook Street, Winnipeg 2, Man.
RICHTER, ROBERT ROY M.D.(Toronto) 1947	46 Sherman Avenue South, Hamilton, Ont.
SIMURDA, MICHAEL ANDREW M.D.(Toronto) 1953	Box 255, Bradford, Ont.
TREDGER, CECIL NORMAN M.D.(Alberta) 1943	1765 - 4th Street, Burnaby 3, B.C.
VIRGIN, WILLIAM JOHN M.D.(Toronto) 1933	19 Caithness Avenue, Toronto 6, Ont.
WAUGH, THEODORE ROGERS JR., M.D., C.M.(McGill) 1953	245 Avenue C, New York 9, N.Y., U.S.A.
WILSON, WILLIAM EVERTON M.D., C.M.(McGill) 1953	27 York Avenue, Watertown, Mass., U.S.A.

SPECIALTY OF OTOLARYNGOLOGY (15)

ANDREWS, PHILIP ANTHONY J. M.D.(Toronto) 1955	Interns' Residence, Toronto General Hospital, Toronto, Ont.
BRISSON, JEAN M.D.(Laval) 1955	190, rue Ste-Marie, Hull, Que.
BROSNAN, MORGAN LEO L.R.C.P.I., L.R.C.S.I., L.M.(Dublin, Ireland) 1950	21 Howard Drive, Willowdale, Ont.
CODERQUE, JUAN ANTONIA M.D.(Zaragoza, Spain) 1953	328 The Heights Drive, Don Mills, Ont.
DESJARDINS, ROGER M.D.(Montreal) 1948	8415, rue Saint-Denis, Montreal, Que.
FARKASHIDY, JOSEPH M.D.(Budapest) 1938	Banting Institute, 100 College Street, Toronto, Ont.
FIALKOV, GERSHON M.D.(Hebrew Univ., Jerusalem) 1954	41 Dorking Crescent, Downsview, Toronto, Ont.
FORTIN, PAUL HENRI M.D.(Laval) 1949	Box 512, R.R. No. 1, Rothwell Heights, Ottawa, Ont.
HENNECKE, THEA-AUGUSTE M.D.(Tübigen, Germany) 1932	1558 Ouellette Avenue, Windsor, Ont.
JOHNSTON, HUGH DOUGLAS M.D.(Toronto) 1955	154 Brant Avenue, Brantford, Ont.
OLEKSIUK, STANLEY M.D.(Ottawa) 1955	1571 Pierre Avenue, Windsor, Ont.
PAGE, GEORGE BENSON M.D.(Toronto) 1952	102 Charles Avenue, Valois, Que.
PHILLIPS, LESLIE JOEL M.B., B.S.(London) 1952	121 - 7th Street, S.E., Medicine Hat, Alta.
RAGAN, TERRENCE MAURICE M.D.(Alberta) 1943	531 - 13 Avenue West, Vancouver, B.C.
REYNOLDS, WILLIAM VINCENT L.R.C.P.I., L.R.C.S.I., (Dublin) 1953	203 Graburn Building, 2nd Street S.E., Medicine Hat, Alta.

SPECIALTY OF PLASTIC SURGERY (4)

FIELDING, JOHN FREDERICK M.D.(Western Ontario) 1954	55 South Kingsway Drive, Toronto 3, Ont.
NORONHA, ALOYSIUS JOSEPH M.B., B.S.(Bombay, India) 1951	117A Glen Road, Toronto 5, Ont.
ROSS, JAMES FREDERICK M.D., C.M.(Dalhousie) 1951	324 Spring Garden Road, Halifax, N.S.
THOMSON, HUGH GORDON M.D.(Toronto) 1954	100 Gloucester St., Apt. 401, Toronto, Ont.

SPECIALTY OF THORACIC SURGERY (1)

LEPAGE, GILLES M.D.(Montreal) 1951	6750, 44e avenue, Montreal 36, Que.

SPECIALTY OF UROLOGY (12)

BERMAN, BENNIE M.D.(Toronto) 1954	345 Bloor Street West, Suite 20, Toronto 5, Ont.
BLAINE, JAMES DELMAR M.D., C.M.(Queen's) 1949	Medical Centre Apartments, Apt. 604A, 2 Emily Street, Winnipeg, Man.
BONNELL, GEORGE ELMER M.D., C.M.(Dalhousie) 1953	c/o W. E. Bonnell, 4840 Sir George Simpson, Lachine, Que.
COLAPINTO, VINCENT M.D.(Toronto) 1952	309 Briar Hill Avenue, Toronto, Ont.
DUXBURY, JAMES HERBERT M.D., C.M.(McGill) 1953	1242 Judge Place, Victoria, B.C.
MACLEAN, NEIL BRUCE M.D.(Manitoba) 1945	1809 Nanaimo Street, New Westminster, B.C.
MANKIEWICZ, STANLEY M.D.(Manitoba) 1956	Ottawa Civic Hospital, Ottawa, Ont.
O'KELLY, FRANCIS MARY MICHAEL M.B., B.Ch., B.A.O. (Ireland) 1954	166 Jameson Avenue, Toronto, Ont.
PELLERIN, CAMILLE M.D.(Laval) 1955	2100, rue Royale, Trois-Rivières, Que.
SPAKOWSKI, WALERIAN JULIAN M.D., C.M.(Queen's) 1955	810 Lancaster Street, Albany, N.Y., U.S.A.
THOMPSON, GORDON DOUGLAS M.D., C.M.(Queen's) 1955	3410 Kent Avenue, Montreal 26, Que.
UGRAY, IMRE KALMAN M.D.(Peter Pazmany Univ., Budapest, Hungary) 1947	445 Lakeshore Road, Apt. 4D, Mimico, Toronto, Ont.

OBITUARIES

DR. PETER SMYTH CAMPBELL, 79, former Deputy Minister of Health for the Province of Nova Scotia, died on February 4 in Wolfville, N.S.

Born and educated in Port Hood, Cape Breton, Dr. Campbell graduated with a medical degree from McGill University in 1916. Before taking up private practice in Port Hood in 1918, he was resident physician at Montreal General Hospital.

In 1923 he became Divisional Health Officer and was named Chief of the department 10 years later. This title was subsequently changed to Deputy Minister of Health. He retired from this position in 1951.

Dr. Campbell received many honours recognizing his work in public health, especially in his fight against tuberculosis. These included life membership in the Canadian Public Health Association and honorary life membership in the Canadian Tuberculosis Society. In 1957 he was elected senior member of the Canadian Medical Association.

He is survived by his widow, five sons and two daughters.

DR. FERNAND GAUTHIER, 46, died suddenly on February 15 in St. Justine Children's Hospital, Montreal, where he had been consultant gynecologist and surgeon for many years.

Born and educated in La Tuque, P.Q., Dr. Gauthier graduated from the University of Montreal medical school in 1941. He interned at St. Justine Children's Hospital, becoming assistant orthopedic surgeon two years later. In 1945 he went to Boston, Mass., where he studied for one year under Dr. Louis A. Phaneuf, gynecologist.

Surviving are his widow, two sons and a daughter.

DR. T. MILTON GREEN, 83, died in Weston Memorial Hospital, Deer Lake, Newfoundland, February 3.

One of Newfoundland's oldest practising physicians, Dr. Green was born in Markham Township, Ontario, in 1878. After graduation in 1908 from the University of Toronto, he went to Newfoundland, where he practised in several different communities before finally settling in Deer Lake.

Surviving are his widow and six sons.

DR. HENRY HERSON, 60, died February 14 in the Queen Mary Veterans Hospital, Montreal.

Born in Montreal, Dr. Herson received his B.A. degree at McGill University, graduating in medicine from the University of Geneva, Switzerland, in 1926.

During World War II, he served in the Canadian Army Medical Corps at the No. 1 Neurological Hospital in England.

Formerly a lecturer in psychiatry at McGill University, he was also a member of the Canadian Psychiatric Association College and the Royal College of Physicians and Surgeons.

He is survived by his widow, a son and a daughter.

DR. STANLEY HORN, aged 69, died at Miami, Florida, January 28. Born in Warsaw, Poland, Dr. Horn received his medical education in France at the Universities of Montpellier and the Sorbonne. He emigrated to the United States in 1928 and practised in New York City. He served as chief of staff in the Department of Physiotherapy at the Bronx Hospital, New York. In 1938 he moved to Sherbrooke, Quebec, where he established the Medical Electrosurgical Clinic.

He is survived by his widow.

DR. HERBERT J. MELANSON, 63, died at his home in Weymouth, N.S., on February 12 after a lengthy illness.

Known as Weymouth's "typical country doctor", Dr. Melanson was born and educated in Corberrie, Digby County, graduating from Dalhousie University in 1926.

During 36 years as a general practitioner, Dr. Melanson was port doctor at Weymouth North and doctor for the Municipal Home at Marshallton. He was also a staff member of Digby General Hospital.

He is survived by his widow, son and daughter.

DR. ALEXANDER J. MURCHISON, 63, died suddenly at his home in Charlottetown, P.E.I., on February 18.

Born at Clyde River into a family of established doctors (father and uncle), Dr. Murchison graduated from Dalhousie University Medical School in 1928, completed postgraduate studies in New York and British Columbia, and in 1945 received a certificate in psychiatry.

He was active in many medical associations, including the Canadian and American Psychiatric Societies.

He is survived by his widow and two sons, one a third-year medical student at Dalhousie University.

DR. JAMES PULLAR, 91, died in Deer Lodge Hospital, Winnipeg, on February 9.

Born in Scotland, Dr. Pullar emigrated to Winnipeg in 1880, where he obtained an Arts degree and graduated from Manitoba Medical College in 1897.

He served overseas with the No. 4 Canadian Casualty Clearing Station in World War I. R.M.

DR. LESLIE O. SKEELES, 73, obstetrician and gynecologist, died February 18 at the Toronto East General Hospital.

Born and educated in Toronto, Dr. Skeeles graduated from the University of Toronto Medical School in 1911 and interned at St. Michael's Hospital, Toronto. He practised for 45 years at his Gerrard Street East office before retiring in 1959. During World War I, he served overseas with the Royal Army Medical Corps.

He was a charter member of the Toronto East Medical Association, life member of the Academy of Medicine and one of the first staff members of the Toronto East General Hospital department of obstetrics and gynecology.

Surviving are his widow and two daughters.

DR. GEORGE SLOCOMBE, 66, of Port Dover, Ontario, died February 12 in the Hamilton General Hospital.

Born and educated in Port Dover, Dr. Slocombe graduated from the University of Toronto Medical School in 1921. During World War II he was attached to the Royal Canadian Army Medical Corps as Captain and saw active service overseas.

Surviving are his widow, three daughters and a son.

DR. AZRA BESON WICKWARE, 80, died at his home in Tomahawk, Alberta, on February 8. Born in Morrisburg, Ontario, he was a druggist before graduating from Queen's University Medical School in 1913.

His medical appointments included attending physician with the Grand Trunk Railway and rural government doctor in Edmonton.

Surviving are two sons and two daughters.

DR. WILLIAM H. WILLSON, 88, died in Deer Lodge Hospital, Winnipeg on February 12.

Born in St. Catharines, Ontario, he went to Winnipeg as a boy, and was educated there and at the Royal Military College, Kingston. After graduating from the Manitoba Medical College in 1898, he practised for several years in Nelson, B.C., serving overseas during World War I.

He is survived by three sons. One, Dr. Glenn Willson, practises in Flin Flon, Manitoba. R.M.

Canad. M. A. J.
April 8, 1961, vol. 84

BOOK REVIEWS

HUMAN NUTRITION—HISTORIC AND SCIENTIFIC. Monograph III. Institute of Social and Historical Medicine, The New York Academy of Medicine. Edited by Iago Galdston. 321 pp. International Universities Press Inc., New York, 1960. $6.00.

The content of this volume largely precludes presentation of its essence in "capsule" form. The text is made up of papers (some quite brief) presented at an Arden House Conference in 1959, under the auspices of the New York Academy of Medicine. Its Director, Howard Reid Craig, M.D., keynotes the project in a foreword in which he states, "Physicians, as health maintenance personnel and as individuals dedicated to efforts to restore health, should be the first to grasp the importance of knowing the valid facts of nutrition as they are today." The 21 contributors include physicians, anthropologists, researchers and academicians.

Readers will appreciate the book more for the questions it raises than for the answers it provides. Its orientation is such that attention is focused on interpenetration of various elements of nutrition—health situation rather than on data in particular conditions.

Of the 21 items, 12 may be classed as "historical-epidemiological", six as "research-scientific", and three as "mixed". "Food and Food Habits in Alaska and Northern Canada" (Vilhjalmur Steffansson); "From Lavoisier to Beaumont and Hopkins" (E. W. McHenry); and "From Hopkins to the Present" (Elmer V. McCollum) are notable in the first group. In the second, significant findings are discussed in "The Influence of Hormones on Metabolic Demands and Subsequent Alterations in Nutritional Requirements" (Herbert Pollack) and in "Nutritional Factors in the Regulation of Fat Metabolism" (Jules Hirsch and Malcolm L. Peterson).

Speaking as a geneticist rather than as an ex-politician, Henry A. Wallace presents useful insights into applications in agriculture of recently gained knowledge of inheritance; and the effects of such application on the world environment and its human inhabitants. He points out that "Man for 99.99 per cent or more of his life here on earth lived without the benefit of the starchy grains like wheat, oats, barley, rice and Indian corn. . . . Historically, man's body was evolved on the basis of a diet which contains much less starch than the diet of almost any modern man . . .", and raises the question ". . . whether the Oriental, Egyptian, European, Aztec, Mayan and Incan civilizations did not introduce more starch into the diet than man's long history had prepared his body to handle most helpfully." A similar viewpoint is implied in a plea by H. A. Schneider of the Rockefeller Institute, "In brief, then, a philosophy for nutrition in my view should look toward a science of, not physiology or biochemistry, but ecology. And in that ecological context its metaphysic still resides in the presupposition of an ever-increasing list of qualitatively new and distinct entities which are part of the rich fabric of nutritional environment."

This collection of essays is for "sipping" rather than for "gulping". Few prescriptions for malfunction or disease will be found in cut-and-dried form. But much increase in wisdom might be generated by acting on probable impulses toward enquiry and speculation.

CANCER OF THE PHARYNX, LARYNX AND OESOPHAGUS AND ITS SURGICAL TREATMENT. Ronald W. Raven, Westminster Medical School. 292 pp. Illust. Butterworth & Co. Ltd., London and Toronto, 1958. $13.50.

Except for the sections dealing with the nasopharynx and larynx, this book is largely an account of the author's own methods and results in dealing with malignant disease in these organs. It does not purport to provide a general survey of the world literature dealing with these problems, nor does it attempt to assess the role of radiation therapy, except in a very cursory way. Surgical procedures employed by the author are described in a very precise, almost tedious, manner; indeed, it seems hardly necessary to remind the reader that anesthetic is administered, the skin is prepared and suitable sterile drapes are applied before commencing each separate operation. The same tendency to tiresome repetition of minor detail is perhaps the most obvious fault in this otherwise excellent book.

In the section on cancer of the pharynx, there is an interesting chapter on the Paterson-Kelly (Plummer-Vinson) syndrome, which points up our lack of exact knowledge of this condition and of its relationship to carcinoma of the hypopharynx. A tiny chapter on radiation cancer summarizes the published experience concerning pharyngeal tumours apparently induced by radiation therapy for previous benign conditions. The chapters on cancer of the nasopharynx and oropharynx are quite brief, since the role of surgery in these areas is small and the author's experience limited. With cancer of the hypopharynx his experience is extensive. He describes adequately the Wookey two-stage laryngo-pharyngectomy and its variations but, strangely, without reference to Dr. Wookey. His advocacy of concomitant neck dissection is his major contribution to this procedure. His record of seven five-year survivors among 37 patients treated by radical surgical excision is sufficiently encouraging to justify continued application of the method.

In dealing with cancer of the intrathoracic esophagus the author advocates transabdominal mobilization of the stomach with separate right thoracotomy for the esophagectomy and gastroesophageal anastomosis. For lesions of the cardia and lower end of esophagus he recommends a left transthoracic transdiaphragmatic procedure, or for extensive growths a left thoracoabdominal procedure. All these are now generally accepted techniques. When total gastrectomy is required he anastomoses the esophagus to the side of a jejunal loop; it is probable that most surgeons of experience would now employ a single isoperistaltic loop of jejunum with Roux-en-Y reconstruction, or possibly an inset loop of jejunum to join the esophagus and duodenum.

It seems strange that there is no reference whatever to anterior mediastinal reconstruction of the esophagus (Robertson-Sarjeant procedure), or to the use of colonic replacement or bypass.

The author records 48 cases in which he has removed all or part of the intrathoracic esophagus for cancer; the operative mortality was 41%; a single patient has so far lived beyond five years. This seems insufficient

grounds for dismissing radiation therapy in less than one page.

This book is nicely printed and copiously illustrated. It is a useful guide to a difficult and dangerous field of surgical endeavour.

MOTOR EXAMINATION OF PERIPHERAL NERVE INJURIES. Y. T. Oester and John H. Mayer. 89 pp. Illust. Charles C Thomas, Sprinfield, Ill.; The Ryerson Press, Toronto, 1960. $6.00.

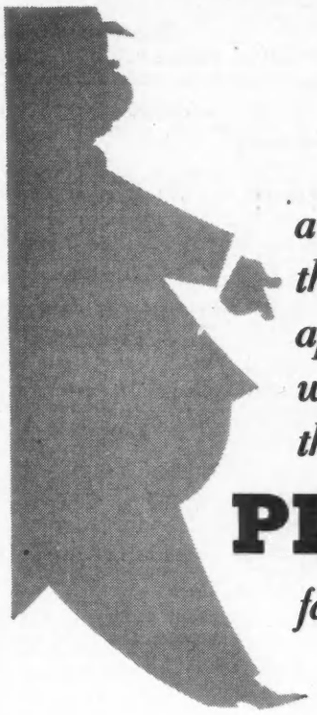
This is a short manual which is designed as a guide for those who are learning how to detect evidence of muscular weakness that results from lesions of the principal peripheral nerves. The action of individual muscles is illustrated by an abundance of photographs. The photographs are not of good quality, but are sufficiently clear to tell their story. A diagram of each nerve and sketches of their cutaneous fields are included. The chief value of the book is derived from its emphasis and excellent illustrations of the "trick" and supplementary movements that usually appear after nerve injury in the upper extremity. The manual is of a handy size, and will be of particular value for the instruction of interns and residents of orthopedic and neurosurgical services.

CANCER OF THE RECTUM. Vol. III, Neoplastic Disease at Various Sites. Edited by Cuthbert E. Dukes. 303 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillian Company of Canada Limited, Toronto, 1960. $8.50.

"Cancer of the Rectum", the third in the series of monographs on "Neoplastic Disease at Various Sites", has now been published. Edited by Dr. Cuthbert Dukes, consulting pathologist to St. Mark's Hospital, London, its 18 contributors are all acknowledged authorities on some particular aspect of cancer of the rectum. Thus the discussions on the pathology of rectal and anal tumours, their diagnosis and treatment, and their postoperative management are of the highest quality. Of great value and interest, too, are the statistical sections of this monograph. The section written by Dr. Cuthbert Dukes on the causation and control of rectal cancer is of most unusual interest. Indeed, this monograph presents in a most scholarly and elegant fashion the great experience of St. Mark's Hospital in the management of cancer of the rectum, its pathology, operations suitable for its treatment, and the postoperative care for patients subjected to operations for rectal cancer. It should be in the library of every surgeon concerned with the treatment of this disease.

THE CELL OF SCHWANN. Gilbert Causey. 120 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1960. $6.00.

This is a short monograph concerning a cell which has attracted the attention of numerous investigators and especially that of electron microscopists. In the past decade many aspects of the morphology of the Schwann cells and of their role in the process of myelinization have been uncovered and clarified. The author, in a clear and concise way, summarizes these recent findings and shows how they confirm, complete or correct the classical descriptions, including the one of Theodore Schwann himself. Thus the first four chapters of the book, dealing with the structure of the nerve fibre as seen with the light and electron microscope, are most instructive. It is unfortunate, however, that the electron microscope photographs do not have



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Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Molecular Genetics and Human Disease. Edited by Lytt I. Gardner. 296 pp. Illust. Charles C Thomas, Springfield Ill.; The Ryerson Press, Toronto, 1961. $12.75.

Facts for Childless Couples. 2nd ed. E. C. Hamblen. 130 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $4.75.

Theory of Shoulder Mechanism. Descriptive and Applied. A. K. Saha. 107 pp. Illust. Charles C Thomas, Springfield, Ill.; 1961. $5.50.

The Tutoring of Brain-Injured Mentally Retarded Children. An Experimental Study. James J. Gallagher. 194 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $7.50.

The Cutaneous Manifestations of the Benign Inflammatory Reticulosis. American Lecture Series. Edited by Samuel M. Bluefarb. 408 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $15.50.

Cerebro-Spinal Fluid Dynamics in Health and Disease. American Lecture Series. David Bowsher. 80 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $5.25.

Medical Forms and Procedures for Industry. Herbert L. Herschensohn. 192 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. $9.25.

Evaluation of Drug Therapy. Proceedings of the Symposium on Evaluation of Drug Therapy in Neurologic and Sensory Diseases held at the University of Wisconsin, May 1960. Edited by Francis M. Foster. 160 pp. The University of Wisconsin Press, Madison, Wis., 1961. $4.00.

Les tractions vertebrales. J. Levernieux. 121 pp. Illust. L'Expansion Scientifique Française, Paris, 1960. 18 NF.

Basic Pharmacology for Nurses. 2nd ed. Jessie E. Squire. 274 pp. The C. V. Mosby Company, St. Louis, Mo., 1961. $3.30.

Tools of Biological Research. Vol. II. Edited by Hedley J. B. Atkins. 175 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $9.50.

Quantitative Cellular Haematology. American Lecture Series. J. M. Yoffey. 122 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $6.00.

COURSE IN

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Mr. William Gissane, Clinical Director, Birmingham Accident Hospital, Birmingham, England.

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"textbook" qualities. Furthermore, there is a lack of explanatory diagrams. The Schwann cell and myelin form such an extremely complex system that it requires such graphic explanations. It would have been interesting to see the area of the node of Ranvier diagrammatically illustrated, as well as the Schmidt-Lantermann incisures, and the structure of the Schwann cells at the level of the nerve endings. These diagrams would have made the book more accessible to the non-specialist. In the following chapters the author arouses our interest in such topics as the development and tissue culture of Schwann cells, their degeneration and regeneration. Here, this reviewer agrees with the author that these topics needed more extensive and detailed coverage.

Such a monograph was amply justified and its reading will be profitable to all those interested in this part of the nervous system.

A STEREOTAXIC ATLAS OF THE DOG'S BRAIN. R. K. S. Lim, Chan-Nao Liu and R. L. Moffitt. 93 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $10.00.

The authors are to be complimented for tackling the difficult job of producing the first atlas on the brain of the dog. This work has been carefully recorded and sources of error are usually duly considered. It might have been more accurate to include a sub-title stating that the measurements described were those of mongrels and beagles; in fact, certain verifications were carried out only on the former. Although these brains might be considered as average for the dog, it might be misleading to use the proportional correlations on the extremes of these species. The figures and the drawings are lucid and are not cluttered with unnecessary details. The reference to specific structures is precise and these can be found readily on the charts. Their distribution and reproduction by the publisher are excellent. The introductory text is clear and, if anything, too concise; the provision of more details about individual variations and interrelation of cardinal structures would seem desirable.

Since the authors' work has involved the use of a well-known and accurate stereotaxic instrument, this atlas will allow many research departments to extend their work to the dog. It is to be hoped that this pioneering effort will be pursued and that the scope of this atlas will be enlarged in future years.

TOWARD THE DIAGNOSIS OF CONGENITAL HEART DISEASE. W. Carleton Whiteside. 86 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $5.00.

In this small book of 85 pages the author has attempted to present a useful guide in the diagnosis of congenital heart disease. The material is arranged under each subject as a series of numbered statements, in the pattern often used by medical students in notes taken at bedside clinical teaching sessions. There is a notable absence of logical progression from history to physical examination to special investigation. The effect on the reader is one of an erratic sequence of poorly related isolated facts.

An unfortunately high proportion of the statements are incorrect. Mistakes in spelling are frequent. There are no formal bibliographic references or acknowledgments in the text, despite the use of prominent cardiologists' names.

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J.H. Toogood et al., Applied Therapeutics, August 1960.

"...dramatic results in **urticaria**... Hydroxyzine combines antihistaminic properties in relieving allergic conditions with muscle-relaxing and tranquilizing effect in allaying the physical and mental stress reactions that accompany these disorders."

Santos, I.M.H. and Unger, L., F.A.C.A., Ann Allergy 18:172 (Feb.) 1960.

"...one of the most effective (tranquilizers) in **chronic urticaria.**" "The relief of itching and hives is often dramatic."

Current Therapy, 1960 Edition, pp. 498.

"...(Atarax) which is also an **antihistamine,** seems to be the most effective in relieving the itchy patient..."

Anning, S.T., F.R.C.P.—Drug Treatment of **Eczema.** British Med. Journal, Nov. 21, 1959.

"A series of 151 allergic patients were treated with (hydroxyzine). The drug was effective in **allergic rhinitis, urticaria, and pruritus** of any allergic cause."

Grater, W.C., Postgraduate Medicine, November 1960.

"...in **chronic urticaria**... The relief of itching and hives is often dramatic."

Eisenberg, B.C., Management of Chronic Urticaria, J.A.M.A., Jan. 3, 1959, Vol. 169, No. 1.

"Pruritic symptoms were relieved by hydroxyzine in 70 of 77 patients with various common skin disorders."

Behling, R., Clinical Medicine, Aug. 1959.

"Overall results show that of seventy-five patients, seventy-two (96%) responded to treatment." "Hydroxyzine is an effective **antipruritic** and tranquilizing preparation with an exceptionally low order of toxicity."

Shapiro, I., Medical Times (Vol. 87, No. 12), December 1959.

"Hydroxyzine hydrochloride... Objective evaluation in 140 patients led to the conclusion that the use of hydroxyzine hydrochloride is valuable adjunctive therapy in the treatment of patients with dermatoses in which emotional tension is a factor."

Robinson, H.R., Jr., Robinson, R.C.V. and Straham, J.F., Southern Medical Journal, Vol. 50, 1282-1287.

"In general the response of **chronic urticaria** to hydroxyzine hydrochloride has been very gratifying and useful."

Bottomley, H.W., M.D., F.R.C.P., Chronic Urticaria, The Winnipeg Clinic QUARTERLY—December 1960.

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PFIZER CANADA

MEDICAL NEWS *in Brief*

(Continued from page 800)

THIRD WORLD CONGRESS OF PSYCHIATRY, MONTREAL, JUNE 4-10, 1961

Many features of the Third World Congress of Psychiatry, which will be held for the first time in the western hemisphere in Montreal, Canada, June 4-10, 1961, will be of interest not only to psychiatrists but also to those in allied fields such as occupational therapy, nursing, clinical psychology and social work. Among these is a panel to be chaired by Dr. Robert H. Felix and comprised of authorities from countries in which national psychiatric programs have been particularly well developed. This panel will deal with the major problems involved in organizing mental hospitals, psychiatric divisions in general hospitals and departments of psychiatry in universities as well as giving close attention to community mental health services, community clinics, school and child guidance clinics, industrial mental health clinics, research laboratories and other facilities.

There will also be a panel discussion on scientific creativity. Outstanding speakers will discuss child development and family problems. An exceptionally large amount of interest will be centred around the new psychopharmacological products, and a series of advance sessions which will be chaired by Professor Jean Delay of Paris.

The Third World Congress, sponsored by the Canadian Psychiatric Association and McGill University, will provide the first opportunity since 1950, when the first Congress was held in Paris, for psychiatrists from all over the world to meet together to discuss the unusually extensive forward movement which has been made in psychiatry during the past decade.

The Congress, expected to attract over 3000 psychiatrists from 62 nations, will embrace all fields of psychiatry in a series of nine plenary and 31 major panel discussions during the week and will give psychiatrists the opportunity to share their discoveries while bringing to the fore major problems of common concern which are still unsolved.

The first plenary session will be concerned with the three major divisions into which the program is divided—phenomenological, experimental and theoretical. Other plenary sessions will deal with more specific subjects – psychotherapy, physical therapies, mental hospitals, concepts and methods in psychiatry, neurophysiology, social psychiatry, child and family psychiatry, and psychopathology.

Simultaneous translations at these sessions will be provided in the four official languages of the Congress – English, French, German and Spanish.

Other scientific sessions will be concerned with such currently important topics as forensic psychiatry, juvenile delinquency, transcultural studies, geriatrics, child psychiatry, genetics, alcoholism and the therapeutic community.

Topics to be covered in more than 400 scientific papers include: addiction, communications, epilepsy, group behaviour, hypnosis, neuroses and psychoses, psychoendocrinology, psychosomatics, drugs, and religion and psychiatry.

Information on registration, reservations and travel may be obtained from: World Congress of Psychiatry, Allan Memorial Institute, 1025 Pine Ave. W., Montreal 2, Canada.

—

CERTIFICATION IN SPECIALTIES: THE COLLEGE OF PHYSICIANS AND SURGEONS OF THE PROVINCE OF QUEBEC

Written examinations in the various specialties will be held in October 1961. To become eligible for these examinations, the candidate must submit, before April 15, 1961, a request describing his postgraduate training and studies.

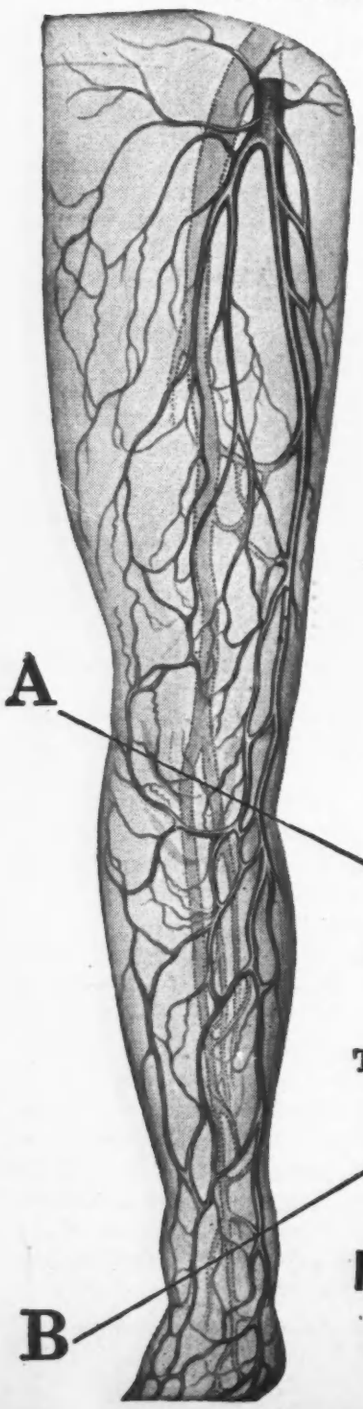
Application forms may be obtained from the College of Physicians and Surgeons of the Province of Quebec. The completed forms, accompanied by all letters and certificates of proof of training, signed by the Medical Directors of the hospitals concerned, must be returned before April 15, 1961, to Dr. Jean Paquin, Registrar, College of Physicians and Surgeons of the Province of Quebec, 1896 Dorchester Street West, Montreal, P.Q.

(Continued on page 40)

THROMBOSIS AND PULMONARY EMBOLISM

Modern way to combat the fourth largest cause of hospital fatalities

The case for T.E.D. Compression stockings as an improved, low-cost method of leg compression



A to B indicates common origin sites of Thrombo-Embolic Disease.

Pulmonary embolism today ranks fourth in incidence of hospital fatalities (perhaps it would be even higher if the cause of death were not often attributed to the accompanying disease).

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In tests conducted at Massachusetts Memorial Hospitals in Boston, the use of T.E.D. Compression Stockings as *standard procedure* (except in cases of ischemic vascular diseases of the legs) reduced the expected incidence of fatal pulmonary embolism by as much as 65%.

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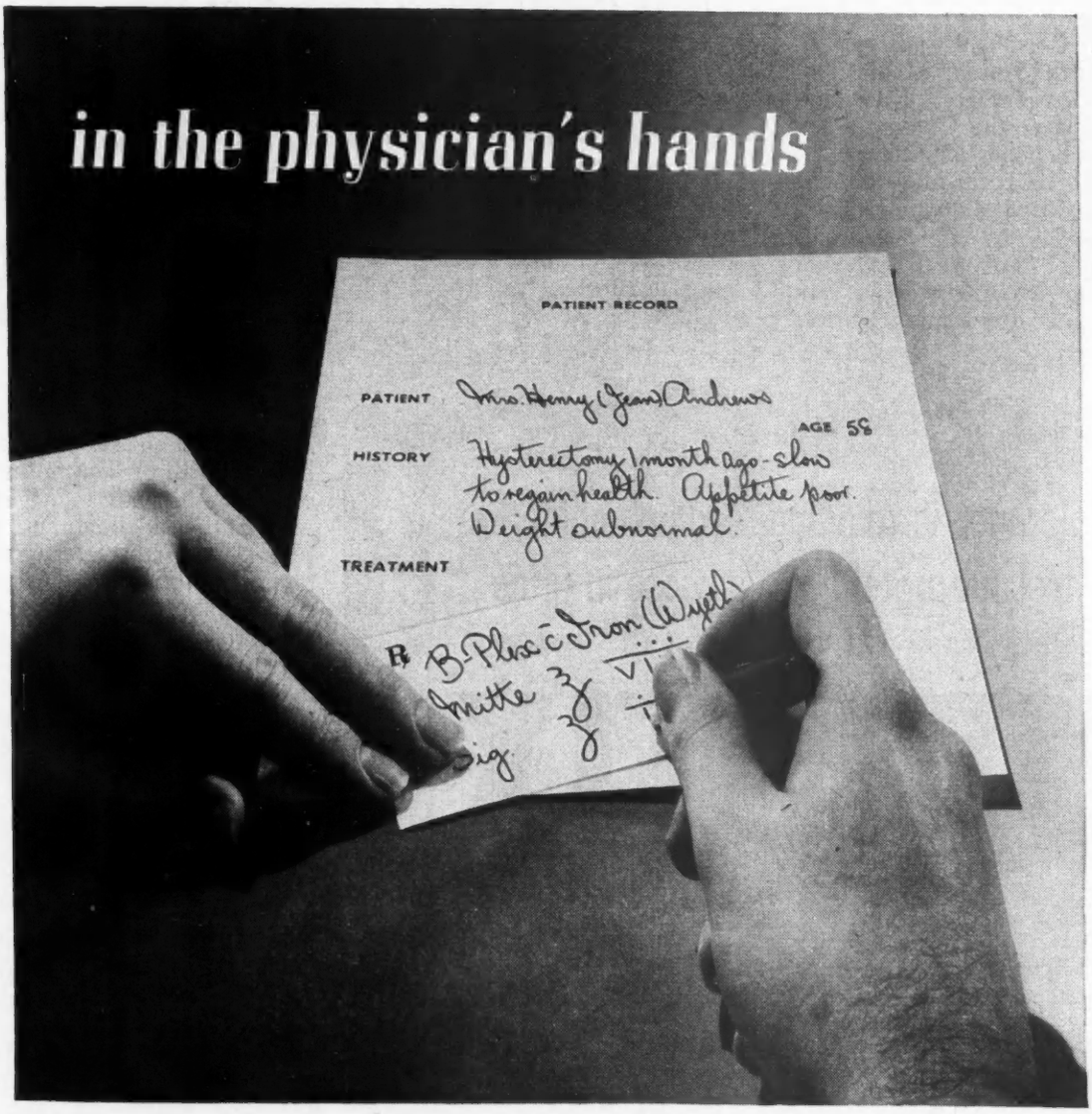

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MEDICAL NEWS *in brief*

(Continued from page 34)

NUTRITION SOCIETY OF CANADA

The fourth Annual Meeting of the Nutrition Society of Canada will be held at the Ontario Agricultural College, Guelph, Ontario, on May 30, 1961, the day immediately preceding the opening of the 1961 meetings of the Canadian Federation of Biological Societies. The one-day meeting will include morning and afternoon scientific sessions and a banquet with a distinguished speaker in the evening. The banquet will be the occasion for the presentation of the second annual Borden Award for an outstanding contribution to nutritional research by a Society member under the age of 40. The first award, presented at the 1960 meeting, was received by Dr. Ian R. Sibbald, of Guelph, for work on energy metabolism and on the conversion of carotene to vitamin A in the chick.

Further information on the Nutrition Society of Canada and its 1961 meeting may be obtained from the Secretary, E. V. Evans, Department of Nutrition, Ontario Agricultural College, Guelph, Ontario. Interested non-members of the Society are welcome to attend the scientific sessions and the banquet.

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NATIONAL TELEVISION PRESENTATION OF FILM ON MENTALLY RETARDED CHILDREN

On Sunday, April 9, from 3 to 3.30 p.m. Eastern Standard Time, The Canadian Broadcasting Corporation will present on its national network the first television showing of the documentary film entitled "One on Every Street". This film, dealing with the problems and care of mentally retarded children, was produced by the Ontario Department of Health and is recommended by those who have viewed it in preliminary screenings as a "bold and honest" presentation of an important health problem.

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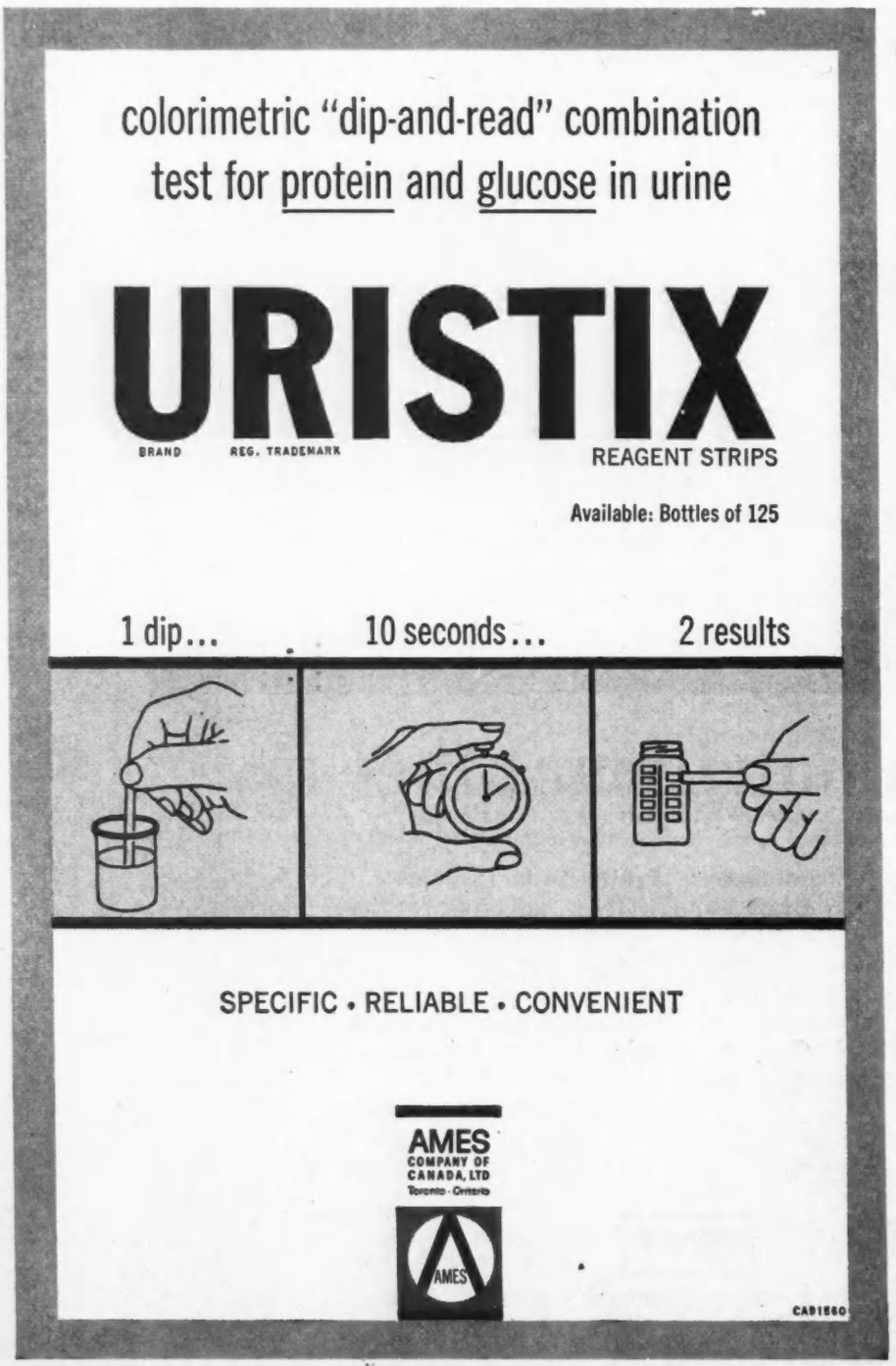
SYMPOSIUM ON PEDIATRIC SURGERY

A Symposium on Pediatric Surgery will be held at the New York University Medical Center, 550 First Avenue, New York, on May 4, 5 and 6, 1961, under the direction of Donald A. Davis, M.D., professor of clinical surgery.

The purpose of this symposium is to present the latest methods and techniques of both diagnosis and surgical management of surgical conditions in the newborn and older children. The program has been planned to attract not only the surgeon but also the pediatrician and the general practitioner, all of whom are interested in improvement in the care of children. The presentation will be in panel form, with authorities in the field of pediatric surgery taking part.

The symposium will feature an exhibit on neonatal intestinal obstructions.

The tuition fee is $75. Further information and applications are available by writing to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, N.Y.